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CHEMICAL SPECIATION AND BIOAVAILABILITY

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Proceedings of the Symposium on the

BIOAVAILABILITY AND DIETARY EXPOSURE OF LEAD

September 1990, Chapel Hill
North Carolina

CHEMICAL SPECIATION AND BIOAVAILABILITY

Aims and Objectives

Chemical Speciation and Bioavailability covers a rapidly expanding area in environmental science. Research on the interactions between the chemical forms and behaviour of toxic compounds and their subsequent biological uptake, metabolism and ecological fate, involves many scientific fields. These studies are often published in discipline-specific journals, leading to inadequate review and information scatter. This situation hinders both the development of an international community of experienced colleagues and the open flow of information and discussion.

Additionally, the importance of speciation and bioavailability research to the development of pollution law and control technologies is being increasingly appreciated by environmental regulatory agencies throughout the world. Besides improving our understanding of fundamental natural processes, results from this research can often be applied to pressing environmental problems such as toxic waste and human health risk assessment.

Chemical Speciation and Bioavailability presents papers in an interdisciplinary forum that explore the chemical, physical, biological and ecological effects of chemical species in the environment. Analytical, legal, and engineering aspects of these species will also be considered.

The following types of communications will be published:

1. Full papers, including reports of experimental results.
2. Short, timely communications.
3. Letters to the Editor.
4. Other types of communications, *e.g.* conference reports, book reviews, will also be considered.

All papers are independently refereed. There are no page charges. The Journal is abstracted by all the major international agencies.

ISSN 0954-2299

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Contents

Preface

The contents of this book are the proceedings of the "Symposium on the Bioavailability and Dietary Exposure of Lead", which was held during September 24–27, 1990, in Chapel Hill, North Carolina.

Over the last several years our increased knowledge of the health effects from exposure to environmental lead has driven researchers to strive for a better understanding of how individuals come into contact with lead, and how the human body reacts to the contact. It is generally accepted that the level of environmental lead to which a person living in the United States is exposed is declining. This is credited in large part to the elimination of leaded gasoline, restricting lead in paint, reducing lead solder in cans for food and water supply lines, and a better understanding of the consequences of lead exposure on the health of humans. It is equally accepted that adverse health effects from lead exposure for particularly vulnerable populations, such as small children and women of child-bearing age, are becoming more apparent, even at significantly reduced levels of exposure. Hence, environmental lead continues to be one of the most significant health-related issues challenging the regulatory agencies who are responsible for the safety and health of our people.

This symposium has successfully brought together two groups of scientists with distinct backgrounds; scientists associated with monitoring lead and other toxic metals in food supplies of their respective nations and scientists and regulators involved with the understanding of the bioavailability of lead from primary soil and dust. The first day and one half of the symposium was devoted to dietary uptake of lead and the remaining two and one half days to bioavailability of lead.

Dietary Exposure

In the mid-1940s, dietary ingestion of lead in the United States was estimated to be 400–500 μg day^{-1}. By the late 1970s, the estimate had dropped to 100 μg day^{-1}, and the more recent measurements in the mid-1980s would indicate a more than ten-fold overall reduction in dietary lead exposure over the last forty years. While highly encouraging, the evidence of health related disease from lead ingestion and inhalation demands that the levels be further reduced.

The dietary exposure program for this symposium was designed to first present a global overview of the levels of toxic metals in the diets of populations around the world, and then provide a forum for discussion of the methods of assessing and monitoring lead in the diets of critical populations. Representatives from Switzerland, Sweden, Yugoslavia, Poland, the United Kingdom, France and the United States attended this symposium to share their experiences and concerns in monitoring and controlling the amount of lead in the diets of the populations of their respective countries and the world. Twenty-five countries have participated in the Food Contamination Monitoring Program, a component of the Global Environmental Monitoring System (GEMS) established by the United Nations Environmental Program.

A broad range of dietary exposures to lead is reported worldwide. Areas of Europe where leaded gasoline prevails were among the countries reporting the highest levels of dietary lead. In several countries, dietary lead alone far exceeds the current joint FAO/WHO provisional tolerable weekly intake of lead from all sources (25 μg kg^{-1} of body weight). In the USA, where dietary lead levels are reported to be the lowest worldwide, it is estimated that 43% of the total exposure to lead for women of child-bearing age comes from their diet. The significance of reducing dietary lead in protecting human health is clearly established.

The program session on assessing dietary exposures to lead in critical populations focused on the methods for measuring consumption and contamination levels of lead in the diets of those populations most vulnerable – the small child and the young woman, particularly those living in high lead-laden environments. A diverse group from the US and abroad presented procedures for assessing exposure from dietary sources. Measurement methodology presented included national 'market-basket' surveys designed to assess the quality of a nation's food supply. Also presented were the more specific 'duplicate diet' techniques aimed at targeting sub-populations where exposure estimates are needed with a high degree of certainty. Of particular interest were presentations concerning the problems associated with obtaining reliable dietary data from inner-city populations and the short-term, high-level exposures associated with storing beverages in, and drinking from, lead crystal.

Bioavailability of Lead

The concept of biological availability as applied to public health risks from environmental pollutants involves risks that are actualised when the substance in a bioactive form is delivered to the sites of toxic action. The specifics of the delivery are modulated by the many factors discussed in this symposium, including the nature of the lead-containing environmental matrix in sources and pathways.

The biological availability of a substance (nutrient, drug or human environmental toxicant) is the fraction of substance entering the systemic circulation (extent of systemic absorption) and the rate at which entry occurs. The bioavailability of environmental lead in human populations is defined by the biological aspects of lead uptake from body compartments, the biophysical–chemical behaviour of different lead species in body compartments, interactive relationships of lead with other species in body compartments and toxicokinetics of lead in the human body. We are here concerned with intake/uptake of exogenous lead, but it should be kept in mind that release of lead from body stores such as the skeleton produces bioavailable lead and endogenous lead exposure.

Biological determinants include (1) interspecies differences, *e.g.* ruminant *vs* monogastric species such as humans, (2) the site of lead uptake in the gastro-intestinal tract, (3) the physiological and molecular processes underlying lead uptake and transport to the systemic circulation from the gut, and (4) the stage of physiological development, *e.g.* children *vs*

adults and young/middle-aged adults vs the aged.

Major topics areas discussed at the symposium and presented here include: issues relating to the bioavailability of lead in soil and dust; animal feeding studies on the bioavailability of lead in soil and dust; and site specific epidemiology studies.

Research Needs

Following the presentation of over thirty papers within seven sessions, the symposium concluded with a panel discussion and audience participation on the research needs and recommendations related to dietary exposure and bioavailability of lead. The following major needs were identified:

1 Additional dietary studies to better identify the levels of lead consumed by small children and to identify the sources of contamination.
2 Improved drinking water data for both consumption and contamination levels.
3 Improved absorption factors of lead for improved modelling of exposure.
4 Determination of the bioavailability of lead from different sources in soil and dust.
5 Improved knowledge of the consequences of sludge compost on environmental lead.
6 Additional information of conversion of insoluble forms of lead in soil at Superfund sites.
7 More study on the physiology of how lead changes as it travels through the intestinal tract.
8 Improved animal model for bioavailability of lead.
9 Development of a dust model for lead.
10 Formation of an oversight panel to advise and coordinate soil lead studies.
11 Database for paint and its inclusion in lead exposure models.
12 Time scales for the recontamination of houses abated of lead.
13 Improved neurological effects data related to blood, bone and brain lead levels.
14 More background lead data for use in the determination of contamination before clean-up activities are deemed necessary.
15 An operational definition of bioavailability.
16 Improved understanding of animal feeding studies and their implication to human health.
17 More information of activity patterns and the interplay between diet and soil consumption.

The symposium coordinators want to thank all of those who supported the symposium. Most especially we acknowledge gratefully the speakers and contributing attendees for their major contributions to the symposium. It was only through their expertise and hard work that the symposium was successful.

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Robert W. Elias
Environmental Criteria Assessment Office, Research
Triangle Park, North Carolina, USA
US Environmental Protection Agency
Program Coordinators

SEGH

The Society for Environmental Geochemistry and Health was formally established on July 1, 1971, as a result of a series of interdisciplinary meetings and symposia. The Society is committed to furthering interest and knowledge of the effects of the geochemical and anthropogenic environment on the health and diseases of plants and animals. Members represent a broad range of scientific disciplines, and reflect a cross section of industry, government and academia.

The Society actively promotes scientific communication and exchange of views among members through conferences, symposia, the journal *Environmental Geochemistry and Health*, a newsletter *Interface* and a series of Monographs. The Society recently sponsored a Lead in Soil Task Force that developed a strategy for regulating and mitigating soil as a source of lead, as well as an international conference on the subject. The current volume is part of a continuing effort to share knowledge concerning the complex nature of lead in our environment. The Society is pleased to be a co-sponsor of this symposium, to facilitate the review of this volume and looks forward to further involvement in fostering research to better understand and deal with the existence of lead in our environment.

C. Richard Cothern
President
Society for Environmental Geochemistry and Health.

Global Overview of Dietary Lead Exposure

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International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Introduction

The joint UNEP/FAO/WHO Food Contamination Monitoring Programme, or GEMS/Food, is a component of the Global Environment Monitoring System (GEMS) established by the United Nations Environment Programme. The major objective of the Programme is to collect, assess and disseminate information on levels and trends of contaminants in food, the magnitude of dietary exposure and significance with regard to public health. At present 39 countries, including the United States of America, participate in GEMS/Food.

Information on the dietary intake of contaminants is of special interest to GEMS/Food since by comparison with tolerable intake levels that have been established a determination can be made as to whether or not consumers are likely to be at risk. In order to encourage international cooperation in such exposure studies, Guidelines for the Study of Dietary Intake of Chemical Contaminants have been published (WHO, 1985). The basic objective of these Guidelines is to aid countries with varying resources to assess the risk of human exposure to chemical contaminants in the food supply. The guidelines provide a detailed description of procedures and methods by which such dietary intake studies may be conducted and have encouraged several countries to conduct such studies and to make available the information to GEMS/Food. Such dietary exposure assessment will enable national health authorities to make sound decision in the regulation of chemical contaminants in food and thus ensure the safety of the food supply with respect to these substances.

Since 1980, a systematic effort has been made to collect information on the dietary intake of various contaminants including lead. The form used for the collection of the data is given in Annex 1. Summary reports of these data have been issued (GEMS/Food, 1986a; 1988; in press) and periodic assessment of these data have been issued out (GEMS/Food 1982, 1986b; UNEP/FAO/WHO, 1988). The GEMS/Food bank is located at WHO, Geneva.

International Recommendations

In 1972, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) established a Provisional Tolerable Weekly Intake (PTWI) for dietary lead of 50 $\mu g\ kg^{-1}$ of body weight, applicable to adults only, and noted that any increase in the amount of lead derived from drinking water or inhaled from the atmosphere will reduce the amount that can be tolerated in food (WHO, 1972). The PTWI was reconfirmed by JECFA in 1978 (WHO, 1978). Because of the special concern for infants and children, JECFA later evaluated the health risks of lead to this sensitive segment of the population and reduced the PTWI to 25 $\mu g\ kg^{-1}$ of body weight. This level refers to lead from all sources. Infants and children are more vulnerable to exposure to lead than adults because of metabolic and behavioural differences (WHO, 1987).

A guideline value of 0.05 mg L^{-1} has been recommended for lead in drinking water (WHO, 1984). This value is at present under review. Within the Joint FAO/WHO Food Standards Programme, maximum levels of 0.2 mg kg^{-1} to 2.0 mg kg^{-1} have been established for lead in a number of foods such as sugars, cocoa products and fruit juices (FAO/WHO, 1984). The International Organization for Standardisation established maximum limits for the release of lead from ceramic ware of 1.7 mg dm^{-2} for flatware and 2.5–5.0 mg L^{-1} of extraction solution for hollow-ware (ISO, 1982).

Dietary Intake of Lead

Adults

Information on the average dietary intake of lead by adults is available from 25 countries. Intake data for the most recent years provided by these countries, varying from 1980 to 1988, are given in Figure 1 and range from 1–63 $\mu g\ kg^{-1}$ body weight $week^{-1}$. Intakes slightly exceeding or approaching the PTWI are reported for the average adult in Cuba (1984), India (1981), Italy (1982) and Thailand (1987). The lowest intake is reported by the USA (1988). There are thus considerable differences in lead intakes reported from different countries. Whether these differences are real or partly due to factors associated with the study approach remains to be assessed. Inadequacies in analytical quality control may also account for some of the differences.

In a 1987 intake study in Australia, the 95th percentile consumption of foods were chosen for the dietary intake calculations to represent the likely maximum intakes (NHMRC, 1990). For the 'extreme' adult consumer, the lead intake was about 17 $\mu g\ kg^{-1}$ body weight $week^{-1}$ or approximately four times the intake of the 'average' adult. Similarly, a mean intake of 25 $\mu g\ kg^{-1}$ body weight $week^{-1}$ reported by New Zealand in 1982 may be partly due to the greater average weight of the diet used in these studies (3.3 kg day^{-1}, excluding drinking water).

As a rough rule-of-thumb, the 95th percentile consumers of food in general have an intake of food that is twice the average consumption of the population as a whole, while the ratio between the mean and the 95th percentile consumption of a particular food appears to be roughly three times the mean consumption (WHO, 1985). Therefore, intake of the average adult population in a country if approaching the PTWI, should be viewed with some concern since a certain segment of the population, because of varying dietary habits, may exceed the PTWI.

In a 1980 study in Denmark, the average adult weekly intake was 8 $\mu g\ kg^{-1}$ body weight. An appreciable increase in

+ Special issue incorporating the Proceedings of the Symposium on the Bioavailability and Dietary Exposure of Lead.

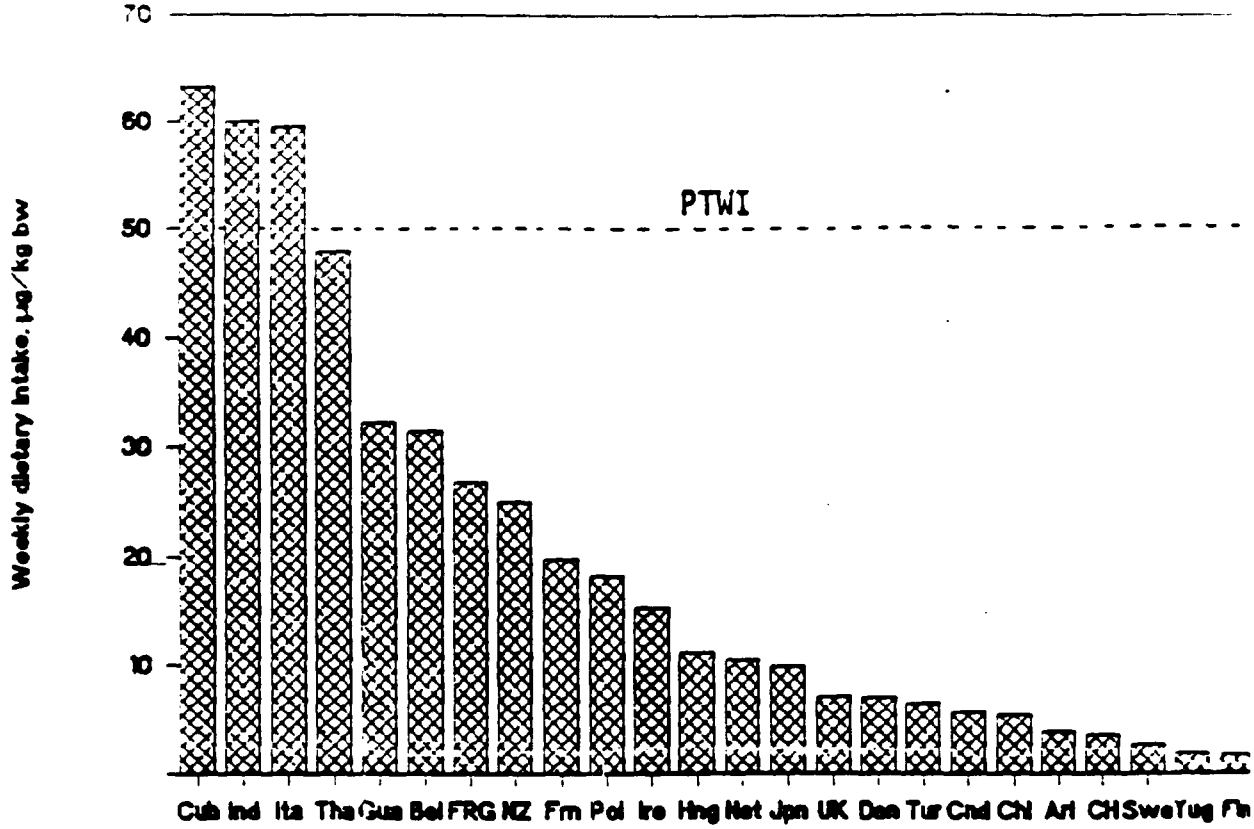

Figure 1 *Average intake of lead. Adults (1980–1988).*

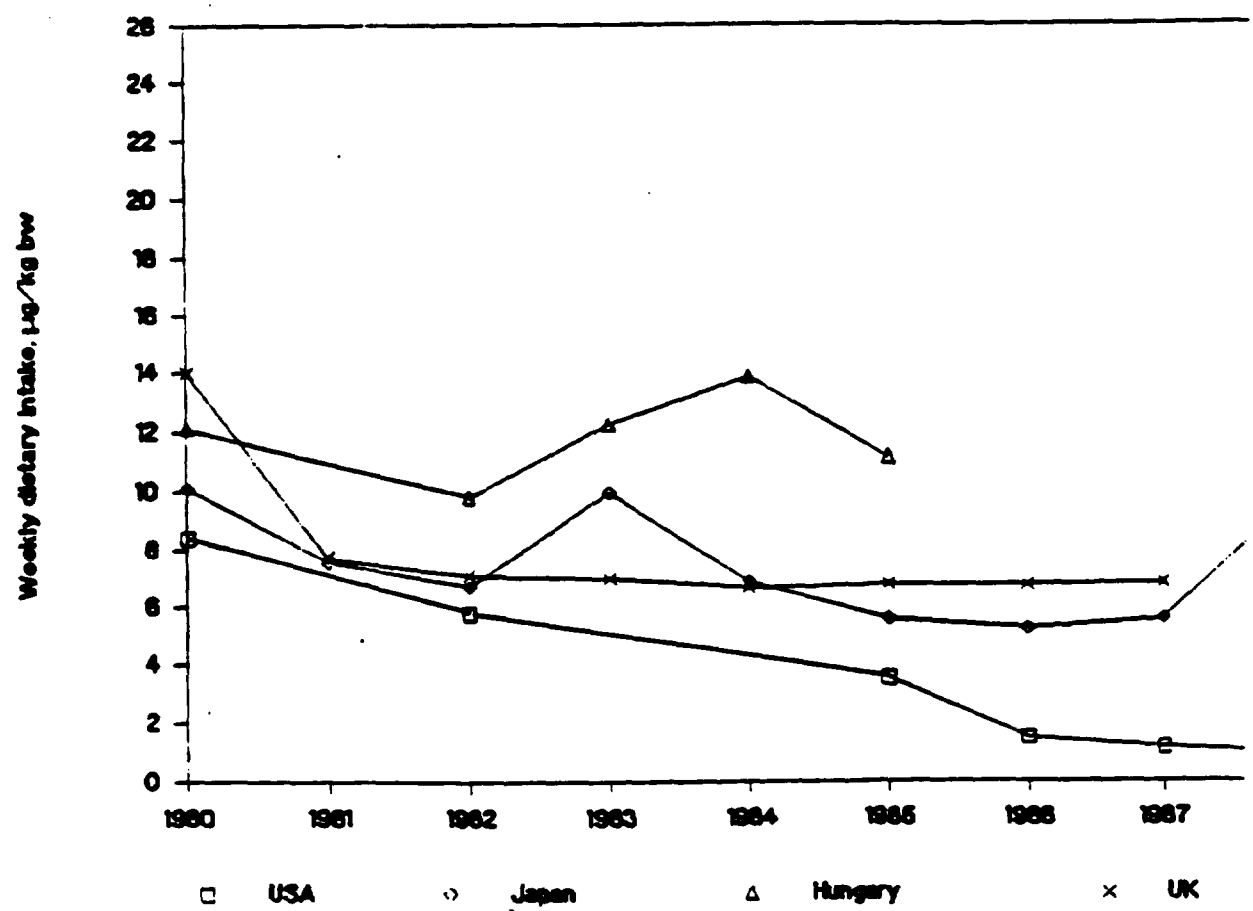

Figure 2 *Trends in lead intake by adults by country.*

Table 1 *Contribution of various foods to the intake of lead by adults as reported by countries.*

Countries	Food	% of total intake
Canada	Vegetables	17
	Meat/fish/poultry	17
	Beverages	15
	Cereals and products	15
	Fruits and juices	10
Denmark	Meat, wine, dairy products and coffee contribute most to lead intake	
Finland	Cereals and products	24
	Fruits	22
	Beverages, sweets, *etc.*	20
	Milk and products	17
	Vegetables	9
Netherlands	Drinking-water	30
	Cereals and products	17
	Vegetables	12
	Wines and spirits	9
	Fruits	6
United Kingdom	Bread and cereals	15
	Beverages	14
	Potatoes	10
	Milk	9
	Canned vegetables	8
Australia	Tea	20
	Meat	8

mean lead intake was noted with consumption of one quarter of a litre of wine per day (23 $\mu g\ kg^{-1}$ body weight $week^{-1}$), in areas where vegetables are grown close to roads with heavy traffic (39 $\mu g\ kg^{-1}$ body weight $week^{-1}$) and in areas where adults are living around a secondary lead smelter near Copenhagen (33 $\mu g\ kg^{-1}$ body weight $week^{-1}$). Data from Poland also indicate that dietary intakes increase in industrial areas.

In a 1981 study in the United Kingdom, the population studied was living in an area where lead concentrations in tap water were considerably higher than average (1.5 $mg\ L^{-1}$). The total intake of lead was 48 $\mu g\ kg^{-1}$ body weight $week^{-1}$ in comparison to a nationwide average of 7 $\mu g\ kg^{-1}$ body weight $week^{-1}$. Some countries have provided dietary intake information to GEMS/Food over several years. Trends in lead intake are shown for some countries in Figure 2.

It appears that a downward trend in lead intake has taken place in the UK and the USA. The decreasing trend in the USA coincides, in the early 1980s, with a drastic reduction in the use of lead-soldered cans and also the lead content of petrol.

Foodstuffs which contribute most to the total intake of lead by adults vary from country to country and have been identified as being alternately drinking water, beverages, cereals, vegetables and fruit (see Table 1). In spite of high levels of lead that may be found in canned foods, because of their relatively low consumption, these were not identified as major contributors to the intake. The situation is different for beverages which may contribute significantly to the intake because of the high volume consumed.

Infants and Children

Relatively few countries report dietary intake of lead by infants and children. The intake by infants and children up to 12 years of age are given in Figure 3. Since the PTWI of lead for infants and young children refers to the maximum intake from all sources (food, water, air, dust, *etc.*), the average intake from food should be well below the PTWI of 25 $\mu g\ kg^{-1}$ body weight to allow for exposure from other media (WHO, 1987). The PTWI is exceeded in Poland (1985), Federal Republic of Germany (1980) and Hungary (1983).

Infants' lead intakes can be strongly influenced by the lead content of water and storage of infant formulas in lead soldered cans. Mean intakes far in excess of the PTWI (in the 100 $\mu g\ kg^{-1}$ body weight $week^{-1}$ range) were obtained in studies carried out in the Federal Republic of Germany (1980) and the United Kingdom (1981) in areas with high lead content in tap water. This increase in dietary lead results from the water added to dehydrated infant formulas and infant cereals, as well as the water which is consumed directly. In a 1987 study in Canada, when ready-to-use formula stored in lead soldered cans was fed to one month-old infants, the intake amounted to 37 $\mu g\ kg^{-1}$ body weight $week^{-1}$ and was thus higher than the PTWI. In several countries, the lowest intake is reported for infants who consume only breast milk.

In Poland, the intake of children living in industrial areas amounted to 33 $\mu g\ kg^{-1}$ body weight $week^{-1}$ and was double that of children living in non-industrial area.

No trends can, as yet, be firmly established for lead intake by infants and children, except in the USA where a decreasing trend is noticeable. (Figure 4).

Levels of Lead in Food and Estimated Contribution of Various Foods to Lead Intake

Lead is one of the most frequently monitored contaminants in food, with about 30 countries in the GEMS/Food network providing extensive data on concentrations in a wide variety of foods. In the monitoring programme, emphasis is placed on staple foods such as cereals and potatoes and on foods that are most likely to contain high levels of lead (canned food, shellfish).

In spite of the very large data base available, very few countries reported results on the same food over several years, thus limiting the possibility of identifying any time trend within a country. Moreover, the specific food items monitored differed appreciably from one country to another, again limiting the possibility of making comparisons between countries.

Nevertheless, the GEMS/Food network provides some indication of the current levels of lead in broad food groups. Figure 5 shows that, in general, spices and herbs, canned food and beverages, are higher in lead content than cereals, fruit,

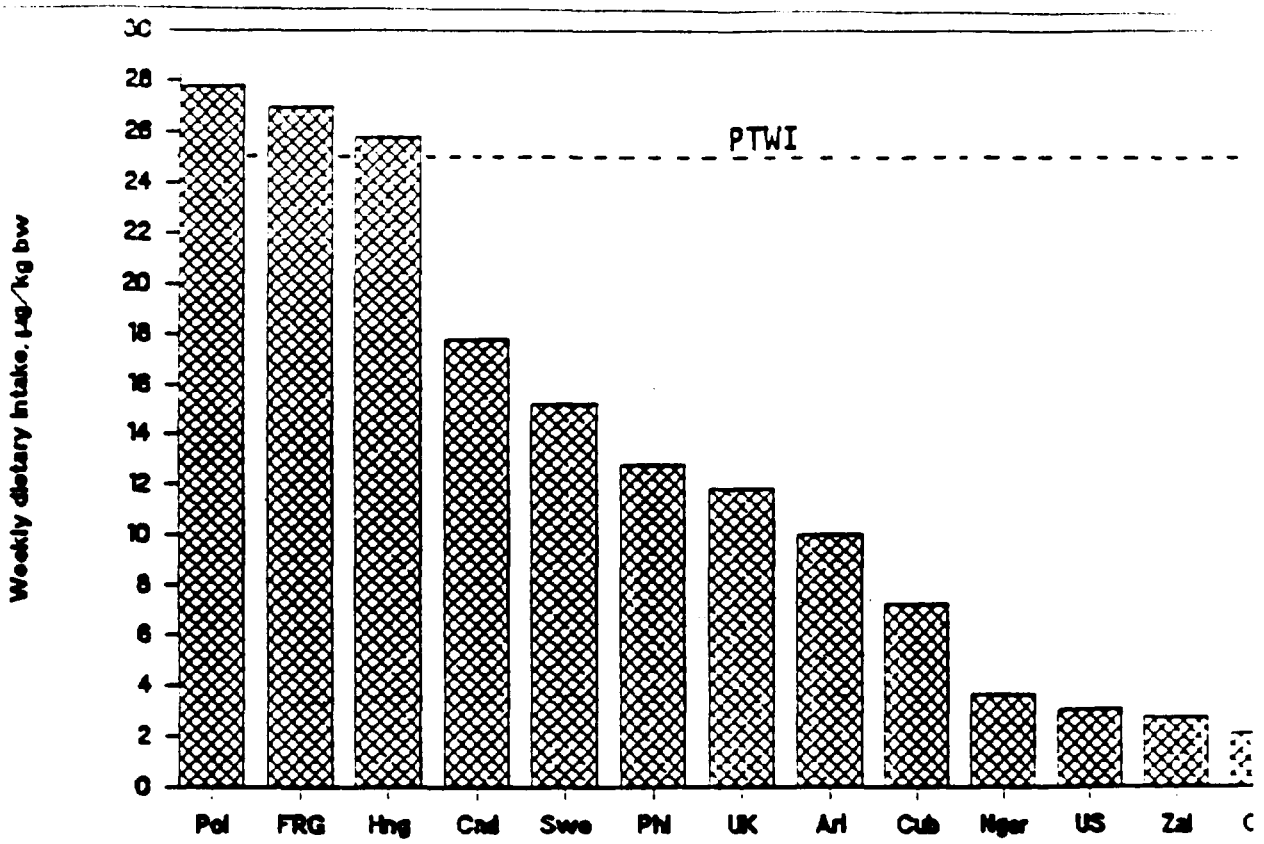

Figure 3 *Average intake of lead. Infants and children (1980–1988).*

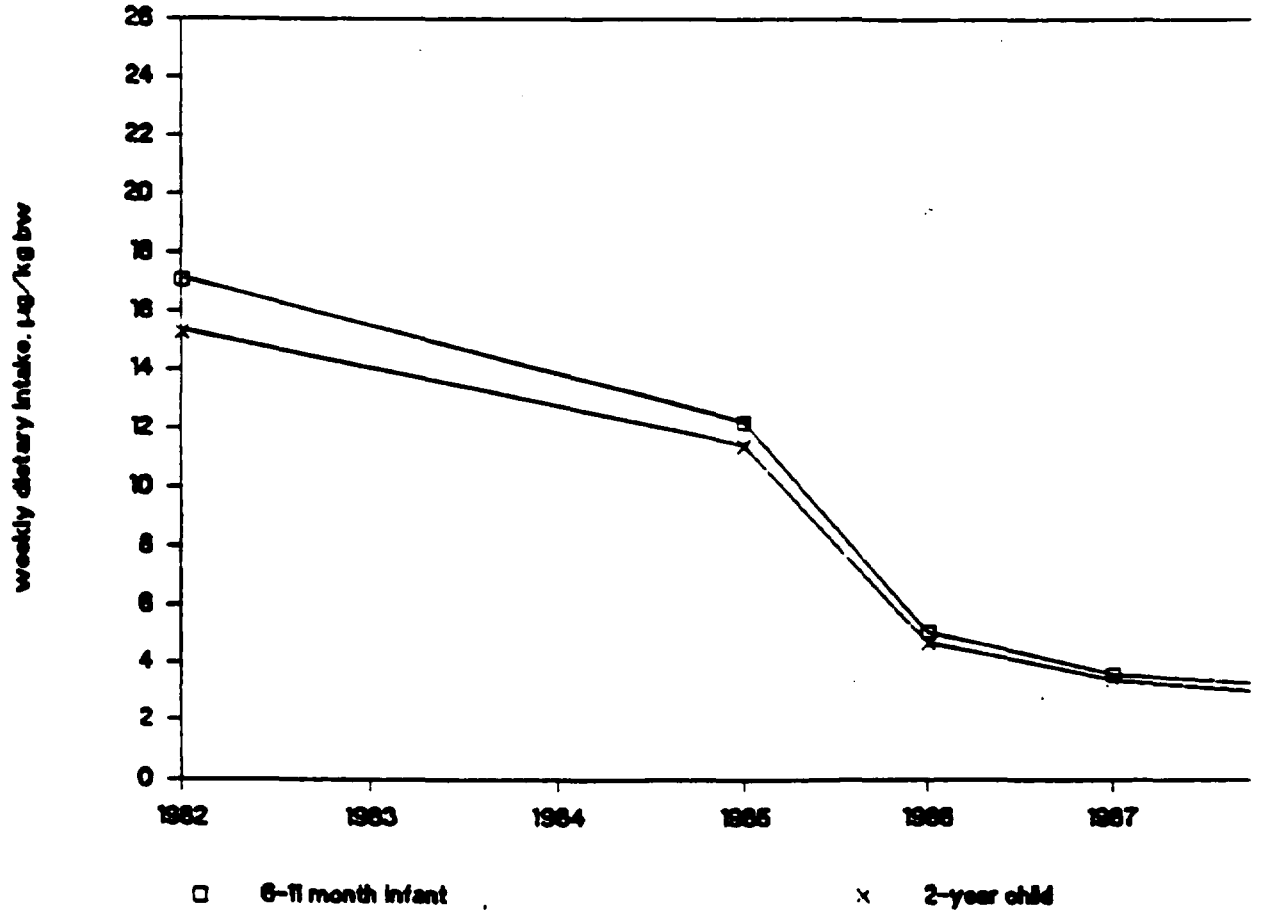

Figure 4 *Trend in lead intake. Infants and children in USA.*

Table 2 *Estimated intake of Pb based on global diet and GEMS/Food data.*

Commodity	Global diet (g day^{-1})	Typical Pb levels (mg kg^{-1})	Estimated intake (µg day^{-1})	% of total
Cereals	405	0.06	24	9.9
Root and tuber	301	0.05	15	6.1
Fruit	236	0.05	12	4.8
Vegetables	182	0.05	9	3.7
Meat	105	0.05	5	2.1
Sugar and honey	58	na		
Milk (solids) and products (eqiv 185 liq. and prod.)	55	0.03	6	2.3
Vegetable oils and fats	38	0.02	1	0.3
Fish	33	0.1	3	1.3
Pulses	22	0.04	1	0.4
Eggs	17	0.02	0	0.1
Nuts and oilseeds	16	0.04	1	0.3
Stimulants	7	na		
Crustaceans and molluscs	6	0.2	1	0.5
Offal	6	0.2	1	0.5
Animal oils and fats	5	na		
Food NES	5	na		
Spices and herbs	3	0.3	1	0.4
Total	1,500	80	32.6	
Drinking water	2,000	0.02	40	16.2
Canned beverages	600	0.2	120	48.7
Canned food*	30	0.2	6	2.4
Grand total			246	100.0
			or 29 µg kg^{-1} body weight week^{-1}	
			(PTWI = 50 µg kg^{-1} body weight week^{-1})	

na – not available.
* – assumes canned food consumption 2% of total.

meat and vegetables. Some canned fruit juices had levels of lead greater than Codex maximum contaminants levels. Further, levels in shellfish are higher than fish and levels in offal are substantially higher than in meat muscle.

Survey data on average contaminant levels in food, together with food consumption data, can be used to obtain rough estimates of intakes. In the absence of dietary intake studies, this approach can be used by governments to make preliminary assessment of likely dietary exposure and to tentatively identify foods that are major contributors to the intake. GEMS/Food survey data, together with a hypothetical 'global' diet are used in Table 2 to illustrate such an approach. The global diet which is representative of an 'average' adult is based on FAO Food Balance Sheets and has been developed following the recommendations of the Joint FAO/WHO Consultation on Guidelines for Predicting Dietary Intake of Pesticide Residues. It is being used to predict intake of pesticide residues (WHO, 1989). This global diet is obtained from the highest average food consumption values from five regional diets and normalising to a total daily consumption of 1.5 kg of solid food, *i.e.* excluding the liquid content of juices or milk.

The contribution of various foods to the intake of a contaminant depends of course on the quantity of the food consumed and the contaminant concentration in that food. In this example, the major contributors to the total intake of 30 µg kg^{-1} body weight week^{-1} are in descending order, canned beverages, drinking water, cereals, root and tuber vegetables and fruit. It is of interest to note that as shown in Table 1 most of these foods have also been identified by several countries as being the major contributors to lead intake. In spite of relatively high levels of lead found in shellfish, offal, spices and canned food, their contribution to the total intake of lead is minimal because they are only consumed at low levels.

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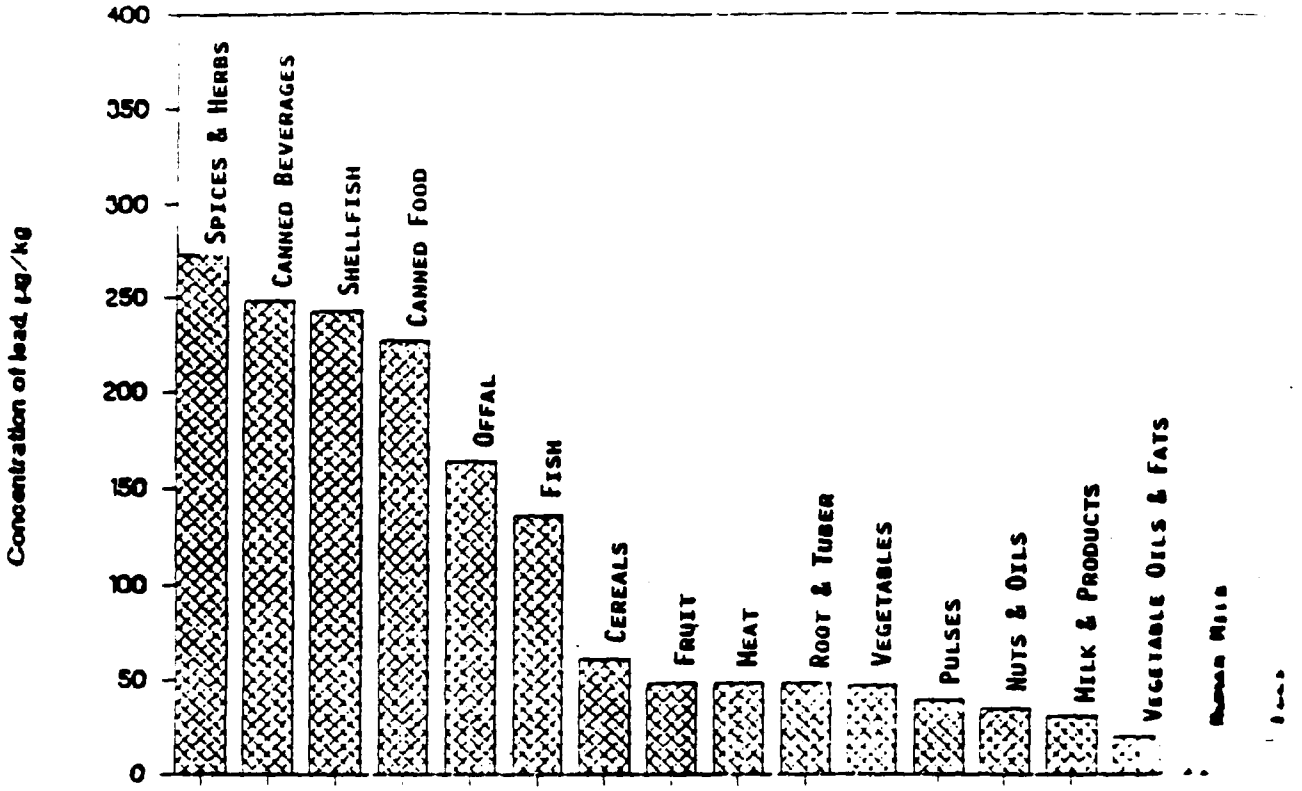

Figure 5 *Typical lead levels in food (1980–1988).*

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H. Galal-Gorchev

(Annex 1)

JOINT FAO/WHO FOOD CONTAMINATION MONITORING PROGRAMME

Serial Number:

leave blank

T | D | | | | | | 1

Dietary Intake of Contaminant Data Form

(see instructions for entering data) Date: _____

1. COUNTRY _____ 8

2. SAMPLING PERIOD____month____year to____month____year. 11

3. TYPE OF DIET:

a.____total diet(give number of composites ____or individual foods ____) 19

b.or____selective studies of individual foods (give number of foods____) 22

c.or___ duplicate portions (entire____, or part___); 25
if part give details in item 17

d.or___other 26

4. TOTAL NUMBER OF FOOD ITEMS INCLUDED _____ 29

5. BEVERAGES INCLUDED__coffee/tea/soft drinks,___drinking water, and/or___alcoholic drinks. 30

6. PREPARATION OF DIET__cooked,__uncooked or___both 31

7. DESCRIPTION OF PERSONS CONSUMING DIET _____ 32

_____

8. AVERAGE BODY WEIGHT _____ kg 35

9. DAILY CONSUMPTION OF DIET _____ g/person/day 38

10. CONTAMINANT _____ 42

11. NUMBER OF DIETS ANALYZED _____ 46

12. MEDIAN CONTAMINANT INTAKE _____ µg/person/day 48

13. 90TH PERCENTILE CONTAMINANT INTAKE _____ µg/person/day 56

14. MEAN CONTAMINANT INTAKE _____ µg/person/day 64

15. ANALYTICAL QUALITY ASSURANCE___yes___no 72

16. RESULTS PUBLICATION (give full reference or attach copy):

_____

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17. REMARKS _____

_____

Dietary Exposure to Lead and Cadmium in Sweden

S. Slorach, L. Jorhem and W. Becker

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Abstract

A duplicate diet study on male and female pensioners in 1970–71 showed mean daily dietary lead intakes of 30 μg and 19 μg respectively. The corresponding cadmium intakes were 10.5 μg and 12.9 μg. Analysis of duplicate diets collected during seven consecutive 24-hour periods from 15 women in Stockholm in 1988 showed a mean daily lead intake of 26 μg (range 13–40 μg). The corresponding cadmium intake was 8.5 μg (range 5.7 - 14 μg). Analysis of faeces samples corresponding to the duplicate diets showed similar lead and cadmium contents (mean lead content 24 μg day^{-1}, range 10–41 μg day^{-1}; mean cadmium content 8.9 μg day^{-1}, range 5.5–12 μg day^{-1}). The median lead and cadmium concentrations in human milk collected in Uppsala were 2 μg kg^{-1} and 0.1 mg kg^{-1} respectively. The median weekly intakes of lead and cadmium by the breast-fed infants were calculated to be 2 μg kg^{-1} body weight and 0.1 μg kg^{-1} body weight. Analysis of seven daily diets, together representing the weekly diet of an adult Swedish male, showed a mean lead content of 26 μg (range 15–45 μg), and a mean cadmium content of 10 μg (range 7–15 μg). The mean daily intakes of lead and cadmium found by analysing market baskets prepared in 1987 were 17 μg and 12 μg respectively. Calculations based on food balance sheet data and levels of lead and cadmium in individual foods showed mean daily intakes of 30 μg lead and 14 μg cadmium per person.

Introduction

In Sweden, dietary exposure to lead and cadmium has been estimated by analysing duplicate diets and market baskets, and by combining information on food intake with data on the levels of lead and cadmium in individual foods. The major studies carried out during the last two decades are reviewed here. In addition, action being taken by the Swedish National Food Administration to reduce lead levels in food is briefly discussed.

Duplicate Diet Studies

Dalby study on pensioners

Schütz (1979) reported the results of the analysis of duplicate diets collected in 1970–71 from 68–69 year-old pensioners in Dalby in the south of Sweden. This was part of an extensive study on nutrition and health in old age. The diets were analysed by flame atomic absorption spectrophotometry after wet ashing, chelation of the metals, and extraction into an organic phase. The results for lead are shown in Table 1, and those for cadmium in Table 2. They show that the female pensioners consumed less food and had a lower intake of both lead and cadmium than the males.

The HEAL study in Stockholm

Exposure monitoring of lead and cadmium was carried out in Stockholm in February–March, 1988, as part of the United Nations Environment Programme (UNEP)/World Health Organization (WHO) Human Exposure Assessment Locations (HEAL) Programme (Vahter and Slorach, 1990; Vahter *et al.*, 1991). Personal exposure via air, food and beverages was measured during seven consecutive 24-hour periods. The study was carried out on 15 non-smoking women, 27–46 years of age, and not occupationally exposed to lead or cadmium.

Duplicate portions of all foods and beverages, including drinking water but not certain medicines and chewing gum, consumed during the entire study period were collected as 24-hour samples. Detailed food records were kept by each participant so that the relation between high lead and/or cadmium intakes and the ingestion of certain foods could be studied. However, the subjects were not asked to record the weight of each food item consumed, since it was feared that the extra work and inconvenience involved would influence their food consumption.

The samples were analysed for lead and cadmium by graphite furnace atomic absorption spectrophotometry (GFAAS) after dry ashing. Extensive analytical quality control was carried out using freeze-dried simulated human diets with a range of lead and cadmium levels (Vahter *et al.*,1990, 1991; Jorhem and Slorach, 1988).

The daily dietary intakes of lead and cadmium are shown in Table 3. There were very wide day-to-day variations in the amounts of lead and cadmium in the duplicate daily diets; this is illustrated in Figure 1. The lead content of the 105 diets from the 15 subjects varied from 4.4–130 μg, and the cadmium content varied from 1.8–56 μg.

From the subject's food record it was possible to correlate high intakes of lead with the consumption of wine or canned foods. Foods packed in lead-soldered cans, and wine, have been shown to contain relatively high lead levels (see, for example, Slorach and Jorhem, 1982; Jorhem, Mattsson and Slorach, 1988).

High intake of cadmium could in many cases be related to the consumption of hand-peeled shrimps. Such shrimps contain parts of the viscera (hepato-pancreas), which contain much

† *Special issue incorporating the Proceedings of the Symposium on the Bioavailability and Dietary Exposure of Lead.*

Table 1 *Daily dietary intake of lead and energy and total diet weight (mean, SD and range) in the Dalby study.*

No. and sex of subjects	No. of diets	Lead (μg)	Energy (MJ)	Total weight (g) Wet	Dry
16 females	33	19	6.6	1658	313
		8.8	1.2	268	53
		6–39	4.7–10.2	1,109–2,270	230–440
12 males	32	30	8.5	2,012	415
		13.6	2.4	484	115
		11–74	5.5–15.9	1,196–3,364	262–775
1 male*	7	58	8.8	2114	421
		21.9	1.61	120	67
		38–86	6.9–11.9	1,988–2,266	329–532

* Subject using tap water with especially high lead concentration.

Table 2 *Daily dietary intake of cadmium and energy and total diet weight (mean, SD and range) in the Dalby study.*

No. and sex of subjects	No. of diets	Cadmium (μg)	Energy (MJ)	Total weight (g) Wet	Dry
9 males	21	12.0	8.2	1,979	405
		6.2	2.0	448	99
		6–35	5.5–11.7	1,196–3,097	262–547
15 females	28	10.5	6.9	1,681	330
		5.8	1.3	251	60
		4–29	4.7–10.2	1,109–2,270	230–440
	1*	86	5.6	1,840	301

* Diet with especially high unexplainable cadmium content. Not included in the calculation of average intake.

higher cadmium levels than the white meat (muscle) of the shrimps (Jorhem, Mattsson and Slorach, 1984). The relationship between the cadmium content of duplicate diets and the intake of hand-peeled shrimps is shown in Figure 2 (from Vahter *et al.*, 1990). The average energy content of the high cadmium diets (7.8 MJ) was about the same as that of diets containing less than 5 μg cadmium (7.0 MJ).

The gastro-intestinal absorption of lead and cadmium in adults is low, in the order of 5–15% on average. Thus the major part of these trace elements present in the diet will appear in the faeces. In addition to the duplicate diets, corresponding faeces samples were analysed for lead and cadmium content to estimate dietary intake. There was a fairly good correlation

Table 3 *Average daily dietary intake of lead, cadmium and energy and diet weight in the HEAL study in Stockholm on 15 non-smoking women.*

	Mean	SD	Range*
Lead content (μg)	26	7.9	13–40
Cadmium content (μg)	8.5	2.1	5.7–14
Energy content (MJ)	7.8	1.3	5.8–9.7
Wet weight (g)	2342	341	1,563–3,03[illegible]
Dry weight (g)	393	52	307–477

* Range of average daily intakes

between the amounts of lead and cadmium in faeces and in t duplicate diets (Vahter *et al.*, 1991). The mean faecal excretic of lead was 24 μg day^{-1} (range 10–41 μg day^{-1}, and that cadmium was 8.9 mg day^{-1} (range 5.5–12 μg day dietary intakes are shown in Table 3.

In view of the large day-to-day variations in the amount of lead and cadmium in the diet, the sampling period fo duplicate diets and faeces should be at least 5–6 days (Vahter *et al.*, 1991).

Human milk study in Uppsala

Larsson *et al.* (1981) determined the levels of lead and cadmium in individual samples of human milk collected in Uppsala, three or six months *post partum* from 41 healthy mothers 2[illegible] years of age. The median lead concentration was 2 μg kg fresh weight (range 0.5–9.0 μg kg^{-1}), and the median cadmium level was 0.1 μg kg^{-1}. The median weekly intake of lead by th three-month old infants was calculated to be about 2 μg kg body weight, and the median weekly cadmium intake about 0. μg kg^{-1} body weight.

Market Basket Studies

Uppsala study on an adult male weekly diet

Slorach *et al.* (1983) estimated the dietary intake of lead an cadmium by analysing seven daily diets, together representin the weekly diet of an adult Swedish male. The diets wer designed using food balance sheet data as regards nutrients an were *not* a recommended diet. The diets consisted of typica ordinary Swedish dishes and were prepared ready fo consumption using common recipes in 1980. They did no contain wine or canned foods. Aliquots of the diets wer analysed by GFAAS. Analytical quality assurance include analysis of US National Institute of Standards and Technolog (NIST) standard reference materials. The average lead conter of the daily diets was 27 μg (range 15–45 μg) and the averag cadmium content was 10 μg (range 7–15 μg). The averag energy content was 11.7 MJ (range 11.6–12.0 MJ) and the we weight was 1,733 g (range 1,499–1,969 g).

Chernobyl market basket study

Some parts of central and northern Sweden received larg amounts of radioactive fallout after the Chernobyl accident i

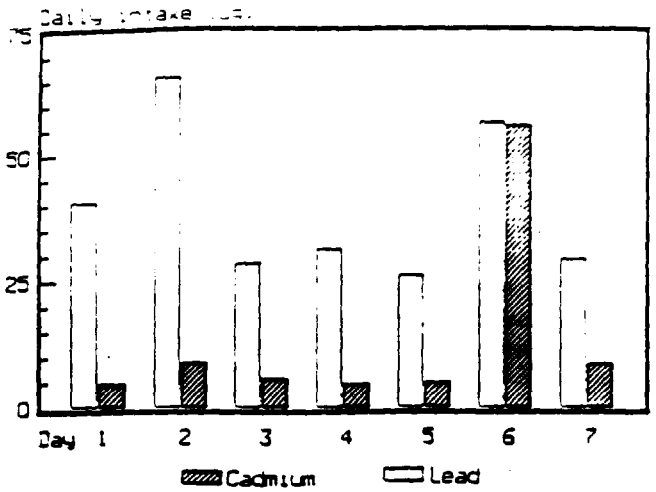

Figure 1 *Example of the day-to-day variations in the dietary intakes of lead and cadmium by one woman during seven consecutive days (from Vahter et al., 1990).*

1986. In order to estimate dietary exposure to radionuclides, market baskets were collected in 1986 and 1987 from eight different towns in Sweden (Becker, Bruce and Ohlander, 1986). The composition of the baskets was based on food balance sheet data. The baskets contained 60 foods and beverages covering 76% by weight of the average total annual *per capita* consumption. All foods for which the average annual consumption exceeds 0.5 kg per person were included. However, because drinking water (and beverages prepared from it) and wines and spirits were not affected by the fallout from Chernobyl, these items were not included. The market baskets did not contain any canned foods and the foods collected were not cooked prior to analysis.

Four of the market baskets (from Malmö, Gothenberg, Stockholm and Sundsvall) collected in the autumn of 1987 were analysed for essential and toxic mineral elements, including lead and cadmium (Becker and Kumpulainen, 1991). The samples were analysed by GFAAS after digestion in concentrated nitric acid. The accuracy of the determinations was confirmed using biological reference materials, including a total diet reference material.

Assuming a daily intake of 2 kg of the market basket, representing an average energy intake of 11.5 MJ, the daily intake of lead was calculated to be 17 µg and the cadmium intake 12 µg. The market basket diets did not contain strong beer, wine or spirits, which were estimated to contribute about 10 µg day^{-1} per person. The total lead intake was thus estimated to be about 27 µg day^{-1} (Becker and Kumpulainen, 1991).

Calculation from food balance sheet data

Becker and Kumpulainen (1991) also calculated the daily dietary intake of lead and cadmium from food disappearance data (*per capita* supply) and data on the levels of lead and cadmium in individual foods. These calculations included the contribution from canned foods, coffee, tea and alcoholic beverages. Based on an energy content of 12 MJ day^{-1}, the calculated lead intake was 30 µg day^{-1}, and the cadmium intake was 14 µg day^{-1}.

Comparison of Results from Different Studies

The studies on the dietary intake of lead and cadmium reviewed above have been carried out using different approaches and refer to different population groups. One way of comparing the results is to express the intakes of lead and cadmium on an energy basis. Such a comparison is shown in Table 4. The results of various studies are in fairly good agreement, especially those for cadmium.

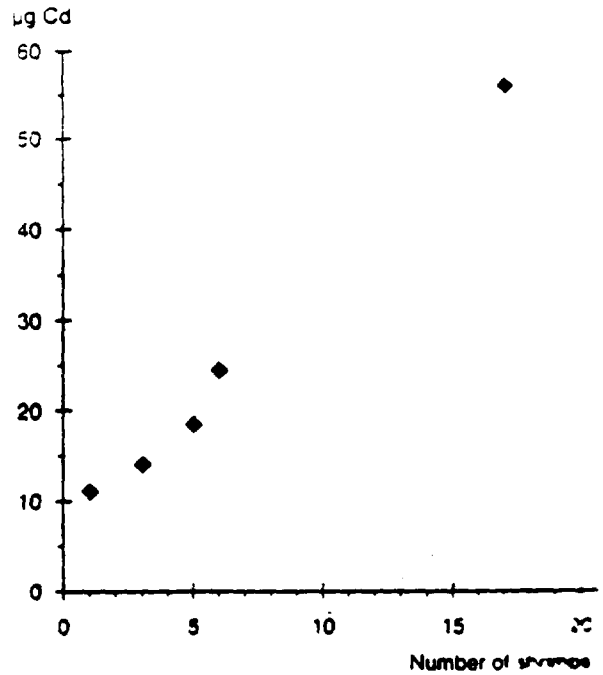

Figure 2 *The cadmium content of duplicate diets in the HEAL study in relation to the intake of hand-peeled [illegible] (from Vahter et al., 1990).*

Future Studies

In 1989, a nationwide Household Food Survey was carried out in Sweden on a representative sample comprising 3,000 households. Four-week records of the household's food purchases, including expenditure and quantities bought, were kept. The results are expected to be available in early 1991. The results of the survey will be used, together with data on the levels of lead and cadmium in individual foods, to calculate the dietary intakes of these metals. In addition, the food survey data will be used when designing new market basket studies.

Reducing Dietary Lead Intake

Compared to the intakes reported from several other countries, the dietary intakes of lead and cadmium found in the Swedish studies reviewed above are low. The estimated average weekly intakes are all well below the provisional tolerable weekly intakes recommended for adults by the Joint FAO/WHO Expert Committee on Food Additives (50 µg kg^{-1} body weight, and 7 µg Cd kg^{-1} body weight; WHO, 1978, 1989). However, in view of the uncertainties regarding the effects of low level exposure to lead on the central nervous system, it is desirable to minimise the exposure to this metal.

Food control agencies can help to reduce dietary exposure to lead by setting and enforcing maximum permitted levels for

Table 4 *Mean lead and cadmium contents of the diets in different studies expressed on an energy basis.*

Study	Lead content [μg (10 MJ)$^{-1}$]	Cadmium content
Dalby – duplicate diets, 1970–71		
Males 68–69 years old	35	16
Females 68–69 years old	29	15
Uppsala, 1980		
Adult Swedish male diet	23	9
Stockholm - duplicate diet, 1988		
Women 27–46 years old	33*	11
Market basket, 1987		
Analysis	15	10
Calculated	25*	12

* Includes wine and canned food.

lead in foodstuffs, and by encouraging those who produce and handle food to eliminate sources of lead contamination. The Swedish National Food Administration is currently reviewing the maximum levels of lead permitted in foods sold in Sweden. A proposal will be issued shortly to lower the lead levels permitted in canned foods, wines and several other foods. In addition, the Administration intends to prohibit the use of lead-containing capsules on wine bottles, and it is considering ways and means of accelerating the phasing out of the use of lead-soldered cans for food. Lead-containing capsules are not used for wines bottled in Sweden, neither are lead-soldered cans used for foods canned in Sweden.

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Dietary Exposure to Lead and Cadmium in Yugoslavia

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Abstract

Lead exposure still represents a matter of health concern especially in Yugoslavia. To assess the exposure of normal urban population to lead and cadmium through food, a preliminary monitoring was performed on a small group of urban population. Lead, cadmium and some essential elements (calcium, zinc, iron, copper and manganese) were analysed in collected duplicate diet samples and compared to similar population in Sweden. We found that dietary exposure to lead and cadmium is similar to other countries although Yugoslav urban population is exposed to much higher concentrations of lead in air than in cities of developed countries, due to high lead in gasoline. However, daily intake of some essential elements was significantly lower.

Also populations living around lead smelters in various parts of Yugoslavia are still exposed to elevated environmental lead and cadmium levels. To assess the exposure of the population living in this area, a cumulative long-term exposure to lead was determined by measuring lead in deciduous teeth. Concentrations of lead and cadmium in vegetables, soil and meals from the same region were also analysed. Values obtained for lead and cadmium in food products grown in exposed and control area were found to be related to respective concentrations of these elements in soil as well as to the distance from the smelter. Meals prepared in this region show the same trend, revealing very high intake particularly of lead.

The influence of nutritional factors, i.e. dietary calcium on lead metabolism, was also studied. Blood lead concentration was determined in two groups of peasant women living in two regions with different dietary calcium intake. Lower blood lead values were found in the higher dietary calcium intake region.

Introduction

In Yugoslavia the environmental lead and cadmium exposure is a matter of concern mainly for two populations living in either urban or lead smelter areas. The former because of leaded gasoline usage (0.6 g L^{-1}) and the high lead content of air and the latter because of highly contaminated soils. When assessing integrated lead and cadmium environmental exposure, the daily diet is one aspect which has to be considered. This aspect is important especially for higher risk population groups (such as infants and young children). In this group higher absorption of lead and cadmium from the gastrointestinal tract was found. Adequate nutrition is also considered to be important in absorption and retention of ingested metals and has also been recommended as a possible preventive measure for protection in conditions of increased environmental exposure. Calcium level as well as the level of some other essential elements (Zn, Fe, Cu, *etc.*) have received special attention (reviewed by Mushak on this symposium).

In this paper results of dietary exposure to lead and cadmium in two different regions, urban and lead smelter are given. Also some evidence of the influence of other dietary components on absorption of lead is presented.

Methods

Lead and cadmium in duplicate diet samples, meals and vegetables were analysed by electrothermal and flame atomic absorption spectrophotometry (AAS), respectively. Analytical quality control and a detailed description of the method were published in the final report of the HEAL project (Vahter, 1990). All the essential elements in duplicate diet samples were analysed by flame AAS. Lead, iron and copper in deciduous teeth were determined by electrothermal AAS and zinc was analysed by flame AAS as described earlier (Ivicic and Blanuša, 1988; Blanuša *et al.*, 1990b). Soil samples were digested with concentrated HNO_3 and lead and cadmium analysed by flame AAS. Blood lead analysis was performed by electrothermal AAS method as described by Vahter (1990).

Results and Discussion

Dietary lead and cadmium in urban area

Within the pilot study Exposure Monitoring of Lead and Cadmium, of the WHO/UNEP Human Exposure Assessment Location (HEAL) Programme, an international intercomparison between four cities (Stockholm, Beijing, Jokohama and Zagreb) on daily dietary lead and cadmium ingestion was performed. A total number of 119 samples of duplicate diet was collected by a selected group of 17 non-smoking female subjects during 7 consecutive days in spring 1988 in Zagreb. Mean daily ingestion of lead was found to be 15 µg and of cadmium 8.5 µg. These values were found to be even lower as compared to some other cities (Beijing and Stockholm) included in the project, inspite of much higher breathing zone air concentrations of these elements in Zagreb (Vahter, 1990).

In two cities (Stockholm and Zagreb) additionally other essential elements, zinc, copper, iron, manganese and calcium were also analysed in the same duplicate diet samples (Blanuša

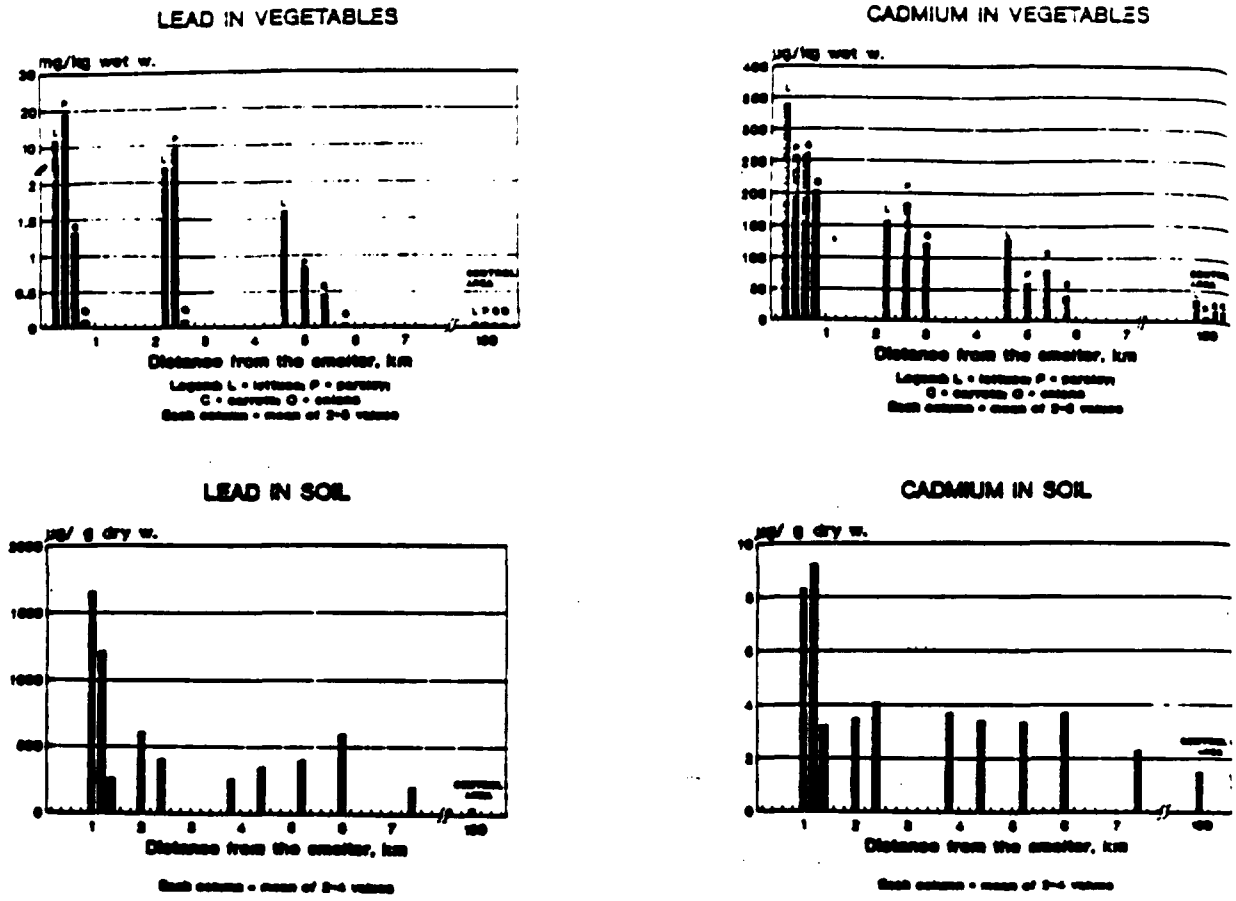

Figure 1 *Lead and cadmium concentrations in vegetables and soil in relation to distance from the lead smelter*

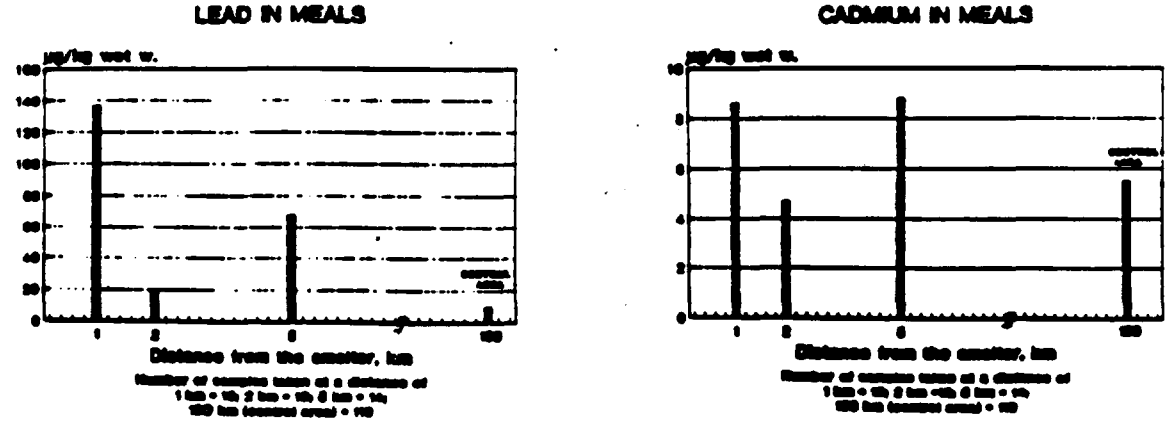

Figure 2 *Lead and cadmium concentrations in meals prepared in homes of local people living in lead smelter area.*

and Jorhem, 1990). While the concentrations of these elements except iron and manganese in diet were approximately the same in Zagreb and Stockholm, the daily intake quantities were however significantly lower in Zagreb than in Stockholm for all elements with the exception of zinc.

Dietary lead and cadmium in lead smelter area

In the north region of Yugoslavia where a lead smelter is situated, the soil is still heavily contaminated. Significant amount of lead and cadmium remain in soil even 10 years a the reduction of smelter lead air pollution. Meals, vegetab and soil samples were collected at different locations in t area. Collected meals were prepared either at homes of lo people or in the kindergardens and school kitchens. Vegeta and soil samples were taken from the gardens of people liv in the region. Concentrations of lead and cadmium found meals prepared at homes were significantly higher than in control region. Means and standard deviations for lead w

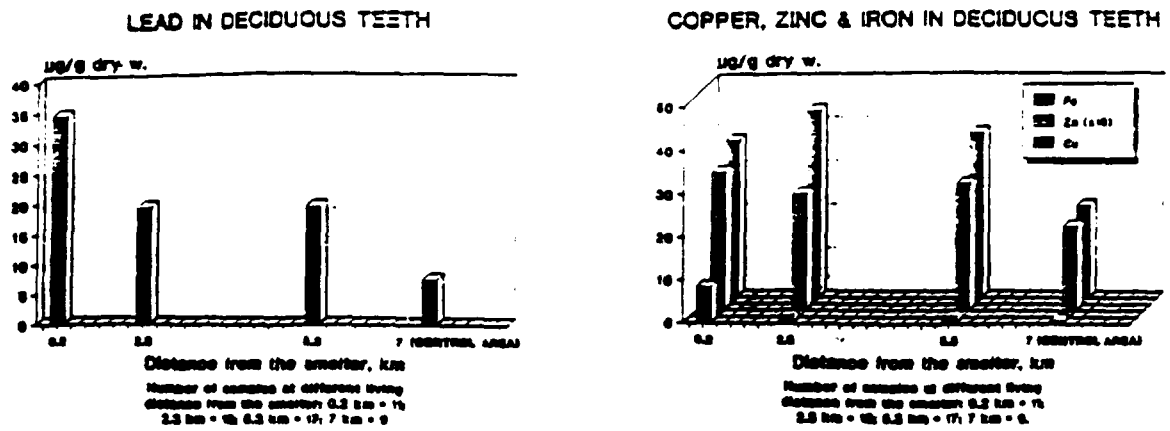

Figure 3 *Lead, iron, zinc and copper concentrations in deciduous teeth of children living in lead smelter area.*

75 ± 105.9 in exposed and 9.9 ± 3.8 in control area and for cadmium 7.3 ± 3.7 and 5.9 ± 2.5 mg kg^{-1} wet weight, respectively. Meals prepared in the school canteens were significantly higher only in lead (16.9 ± 4.3 µg kg^{-1} wet weight) but not in cadmium (5.5 ± 1.7 µg kg^{-1} wet weight) compared to control. The elevation in lead concentrations in the exposed area was much higher in meals prepared at homes than in meals prepared in the school canteens. Concentrations of both elements in soil were significantly higher in the contaminated area than in the control area. The concentrations were 585 ± 479 as compared to 27 ± 8 (lead) and 4.5 ± 2.4 as compared to 1.5 ± 0.5 µg g^{-1} dry weight (cadmium) in soil in the contaminated versus the control region, respectively. All these results presented in relation to the distance from the smelter, show a negative relationship (Figues 1 and 2). Therefore the population living in this area is exposed on the average to 7.6 times higher level of lead and to the same level of cadmium in food compared to the control population (Blanusa *et al.*, 1990a).

Within a WHO study of the Neurotoxic Effect of Lead in Children, lead in deciduous teeth of children living around the same lead smelter was taken as an indicator of the body burden of lead. We analysed not only lead in teeth but also some other parameters such as quantity of ash and concentrations of iron, zinc and copper (Blanusa *et al.*, 1990b). Deciduous teeth of 40 children in exposed and nine children in the control area aged 6–8 years were included. Prior to any statistical evaluation it was evident that when concentrations of elements were related to living distance from the smelter (Figure 3) a negative relationship was obtained. Exploratory principal components analysis was applied as a statistical approach to evaluate the association of eight parameters (lead concentration, lead quantity, zinc, copper and iron concentrations, percent ash, age and living distance from the smelter) at a total number of 49 observations. The analysis showed that three factors were significant: the first factor, 'lead factor', associated closely lead and zinc concentrations in teeth with the distance from the smelter, second factor, 'transmission metal factor', connected iron, zinc and copper and the third, 'mineralization factor', associated age and ash. This logical association of parameters indicated that deciduous teeth might not be only an indicator of the body burden of lead but also an indicator of environmental exposure to some other trace elements or interaction of lead with other elements in the body.

A negative correlation between tooth lead concentration and the residence distance from the smelter as well as between lead in vegetables, soil or meals and the distance, confirm that daily diet is a significant source contributing to lead body burden. It is difficult to assess the quantitative relationship since other sources than food contribute also to lead body burden, especially in children.

Although cadmium was also found to be elevated in soil and vegetables, prepared meals were not significantly different from controls. Therefore cadmium body burden is not expected to be elevated in people living in that particular lead smelter region.

Nutritional factors

The environmental exposure to lead and its absorption is supposed to be influenced by dietary calcium but very few human data are available. This hypothesis was tested by measuring blood lead concentrations in two groups of peasant women living in similar conditions in two different regions in Yugoslavia (100 women in each) with no known lead contamination. In one region the dietary calcium, tested by nutritional interviews (Matkovic *et al.*, 1979), was about 940 mg day^{-1} and in the other about half as much, *i.e.* about 450 mg day^{-1}. The average blood lead concentration was found to be significantly lower (69 ± 4 µg L^{-1}, mean ± SEM) in women from the 'high' calcium region than from the 'low' calcium region (83 ± 4 µg L^{-1}). This finding presents new evidence on the effect of nutritional factors on the metabolism of toxic metals indicating that an adequate diet might be a preventive measure for reducing lead absorption in humans (Kostial *et al.*, 1991).

Conclusions

The conclusions to all these studies are the following:

- In the examined urban population the daily dietary lead intake was not higher than in some other cities, inspite of much higher lead levels in air. The reason might be the

food which comes to the market from suburban unpolluted areas.

- The population living around lead smelters with contaminated surrounding resulting from the past pollution is still exposed to elevated lead levels in food. This is mostly due to preparation of meals with nutrients from local sources.
- Deciduous teeth were shown to be a good indicator of the body burden of lead and possibly also an indicator of environmental exposure to other trace metals or interaction of lead with these elements in the body.
- Dietary calcium intake was shown to influence the blood lead levels in humans indicating the significance of nutritional factors in estimating monitoring results.

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Dietary Monitoring Studies on Lead and Cadmium Exposures in Poland

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Abstract

The dietary intake of metals, especially lead and cadmium, in some regions of Poland exceeds Provisional Tolerable Weekly Intake (PTWI) allowances established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). This is mostly due to increased environmental pollution.
The results of dietary monitoring studies to determine the heavy metals content in daily diets and in selected food products are described.

Introduction

Lead, cadmium and mercury are metals that are potentially the most hazardous to human health. Excessive level of heavy metals in the environment has been associated with the etiology of a number diseases, and especially with cardiovascular, kidney, nervous system and bone diseases; abnormal development of children; mutagenic and teratogenic changes; as well as neoplastic diseases (Nikonorow and Urbanek-Karlowska, 1987).

The main source of toxic metals intake for the general population can be food. Food contamination comes mainly from the emission of polluting substances within areas that have a high density of industrial centres, particularly smelters and heat and power generating plants. The combustion gases from gasoline engines are also a large source of lead emission in Poland. Near highways with heavy traffic, a significant cadmium pollution also occurs because of the cadmium content of car tires. Also, important sources of pollution are the rivers, canals and other surface waters. For example, the lead concentration in the Vistula River is as high as 0.25 mg dm^{-3}, while the allowed limit is only 0.1 mg dm^{-3}.

Another important factor contributing to high metals content of foods is soil contamination resulting from the wide use of fertilizers that are often contaminated with toxic metals, since Polish law does not limit the metal content in fertilizers. Industrial waste and sewage sludge are also used as fertilizers. Results from studies on industrial waste have shown that lead and cadmium content in waste from mines and smelter plants used as fertilizer exceeded 30 g Pb kg^{-1} and 450 mg Cd kg^{-1} (Uminska, 1988). Industrial waste plants and garbage yards are another large source of soil contamination. In Poland, like in many countries, the allowed levels of heavy metals in soil have not yet been established.

Environmental pollution of air, water and especially of soil has a considerable impact on the levels of metals in food. This occurs directly in agriculture crops but also indirectly in meat products.

Limits for Toxic Metals in Foodstuffs in Poland

Poland's major law limiting heavy metals in foods is the Regulation issued by the Ministry of Health and Social Welfare (Monitor Polski No. 45, 1990). The Regulation specifies the limits for the following metals: lead, cadmium, arsenic, copper, zinc, tin and iron. The maximum permitted levels of these metals in foodstuffs in Poland are presented in Table 1. The list does not contain vegetables, fruits and grains, because permitted levels of metals for these products are currently being established. Therefore, these products are categorized as 'others' based on their dry mass content. Vegetables and fruits, for example, are part of the class of products containing less than 20% dry mass (Table 1).

The toxic metals in food may also come from food additives. Therefore, Polish law also limits the levels of particular toxic metals in food additives (Table 2). Permitted levels depend on the content of food additives in a foodstuff (g kg^{-1}). Limits have been established for the following metals: lead, arsenic, mercury, cadmium, copper, zinc and chromium (chromium is limited only in artificial colours).

Dietary Monitoring Studies in Poland

The monitoring studies of food contamination in Poland began in 1968, before the Global Environment Monitoring System (GEMS) project began. Monitoring is supervised by the National Institute of Hygiene, Department of Food Research in collaboration with Regional Sanitary Epidemiological Stations. These studies include determinations in various foods of metals such as lead, cadmium, mercury, arsenic, copper, zinc, tin, selenium and chromium. Results from studies on lead and partly on cadmium are presented. Cadmium is also an important health-risk factor for the general population of Poland. Both studies on the metal content in daily food diets and also in particular food products have been conducted. For example, since 1986 a wide spectrum of studies on levels of heavy metals in agriculture crops have been performed.

† *Special issue incorporating the Proceedings of the Symposium on the Bioavailability and Dietary Exposure of Lead.*

Table 1 *Maximum levels of metals permitted in foods in Poland (mg kg⁻¹) according to Monitor Polski No 45 ...*

Product	Pb	Cd[b]	As	Cu	Zn	Sn[c]	Fe
Dietetic products, baby foods and infant formulas							
Powdered milk	0.1	0.01	0.2	5.0	40.0	15.0	-
Powdered milk formulas	0.1	0.01	0.2	5.0	40.0	15.0	-
Flours and grits used for formulas	0.15	0.01	0.2	6.0	30.0	20.0	-
Canned meat and meat-vegetable products	0.2	0.01	0.2	4.0	30.0	50/20	-
Others[d]:							
Containing below 20% dry mass	0.1	0.01	0.1	2.0	5.0	15.0	-
Containing 20–50% dry mass	0.1	0.01	0.1	5.0	20.0	15.0	-
Containing above 50% dry mass	0.1	0.01	0.2	10.0	30.0	20.0	-
Other food products							
Milk[a]	0.15	0.01	0.1	0.5	5.0	20.0	-
Condensed milk	0.2	0.03	0.2	5.0	20.0	100/20	-
Powdered milk	0.3	0.10	0.2	5.0	40.0	20.0	-
Cottage cheese	0.5	0.05	0.2	3.0	20.0	-	-
Canned meat and meat and vegetable products	1.0	0.05[e]	0.5	8.0	50.0	100/20	-
Canned poultry products	0.5	0.05[f]	0.2	5.0	20.0	100/20	-
Fish products	1.0	0.05[f]	4.0	10.0	50.0	100/50	-
Vegetable oils and fats	0.1	0.05	0.1	0.1	-	-	1.5
Animal fats	0.1	0.02	0.1	0.4	-	-	1.5
Sugar	0.5	0.02	0.2	3.0	-	-	-
Fruits	0.5	0.05	0.5	10.0	20.0	20.0	-
Compotes[a]	0.4	0.03	0.2	3.5	5.0	100/20	-
Juices[a]	0.3	0.03	0.2	3.5	5.0	100/20	-
Canned vegetables	0.6	0.03	0.2	5.0	15.0	100/20	-
Tomato concentrate	2.0	0.05	0.2	15.0	30.0	150/50	-
Flours and grits	0.3	0.10	0.2	6.0	40.0	-	-
Bakery products and macaroni	0.4	0.10	0.2	5.0	40.0	-	-
Soft drinks[a]	0.3	0.03	0.1	1.0	5.0	-	0.5[g] 5.0[h]
Others[d]:							
Containing below 20% dry mass	0.3	0.03	0.2	4.0	10.0	150/20	-
Containing 20–50% dry mass	0.5	0.05	0.2	10.0	20.0	100/20	-
Containing above 50% dry mass	1.0	0.10	0.5	20.0	50.0	100/20	-

[a] mg dm^{-3}.
[b] Limits for Cd for *Other food products* are regulated starting in December 1992.
[c] Metal/other packages.
[d] Valid unless specified for particular products.
[e] Not for products containing liver and kidneys.
[f] Not for products containing liver.
[g] Non-sweetened.
[h] Sweetened.

Table 2 *Maximum levels of metals permitted in food additives in Poland (mg kg^{-1}) according to Monitor Polski No.45, 1990.*

Metal	Additive level in food (<1g kg^{-1})	(>1g kg^{-1})
Pb	5	1
Cd	0.1	0.1
As	3	1
Hg	0.01	0.01
Cu	30	30
Zn	50	50
Cr[a]	2	2

[a] Only for artificial colours.

These results were reported to the WHO - Food Safety Unit, Division of Environmental Health as the Polish participation in the GEMS/Food project and are included in the GEMS reports (GEMS, 1988). As an example, Figure 1 shows the weekly dietary intake of lead for adults in 17 countries, including Poland (Joint FAO/WHO Food Standards Programme, 1990). The adult dietary lead intake in Poland appears slightly above the average intake for the countries included in the program. Another example (Figure 2) describes the weekly dietary intake of lead for infants and children. Studies done in Poland are for children 1–3 years old. Lead intake was found to be similar to those reported by other countries (GEMS, Assessment 1988).

Figure 3 shows the 49 administrative districts of Poland. Regions with high environmental pollution resulting from very dense distributions of factories, smelters and coal mines are localised in the south-west part of Poland. In this area contributions to environmental pollution also come from neighbour countries, especially through air and water. The districts in Poland where studies were performed on whole diet metal intake and metal content in agriculture crops are marked in Figure 3. Moreover, in all districts, the laboratories in the Sanitary-Epidemiological Stations determine the metal content in food products according to Polish standards, as a part of their regular control activities.

The analytical methods used for determination of metals were developed or adopted by the National Institute of Hygiene and are based on atomic absorption spectroscopy (AAS). Lead and cadmium were determined using flame AAS methods after dry ashing (at 400°C) and extraction of metal complexes with ammonium-1-pyrrolidinedithiocarbamate (APDC) to butyl acetate. For copper and zinc, we also used the AAS flame method. Samples were analysed after dry mineralization directly from the solution of residue. A flameless AAS method was used for mercury determination after wet mineralization using a cold vapour technique. These methods were checked against International Standard Reference Materials obtained from the National Institute of Standards and Technology (NIST), USA, and in collaborative studies in Poland.

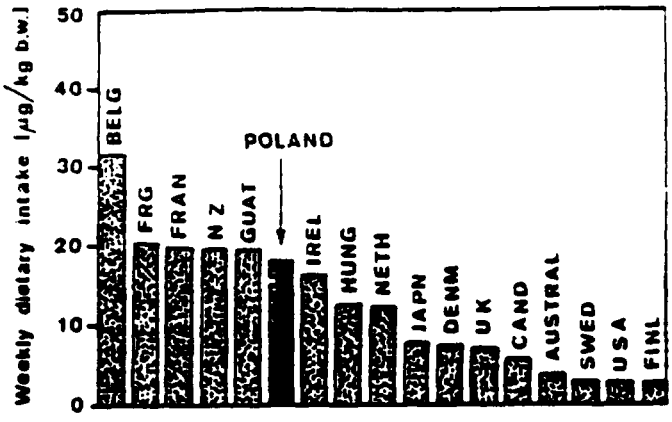

Figure 1 *Avarage intake of lead for adults, 1980–88 (from Joint FAO/WHO Food Standards Programme, 1990).*

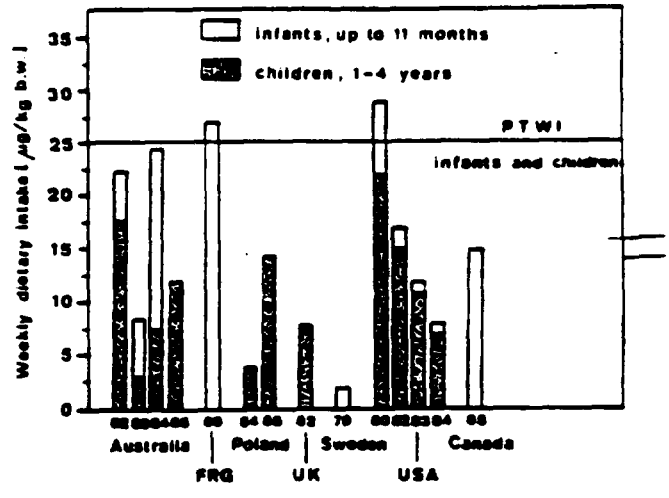

Figure 2 *Median/mean dietary intake of lead for infants and children (from GEMS Assessment, 1988).*

Lead and Cadmium Intake with Daily Diets

The lead, cadmium and mercury intakes from daily diets for selected groups of the Polish population, namely for children 1–3 years old and teenagers 14–18 years old, were studied (Zawadzka *et al.*, 1986, 1987; Ludwicki, 1987). The method of duplicate portions was applied. Studies included 14 districts, representing approximately one quarter of Poland. Samples of daily diets were collected from kitchens of high school dormitories and also from child care and nursery facilities. Food was sampled for the following 10 days in one month of each quarter of the year, for two years. A total of about 1,700 whole diet samples were examined. Results of studies of weekly metal intakes for particular districts are presented in Figures 4–7 in the form of diagrams, presenting arithmetic means, medians and 90th percentile intake.

The average lead intake by Polish teenagers was far below the adult Provisional Tolerable Weekly Intake (PTWI) established as 0.05 mg kg^{-1} body weight by JECFA (WHO, Technical Report Series, 1972). However, meals were found to be significantly polluted with lead in some

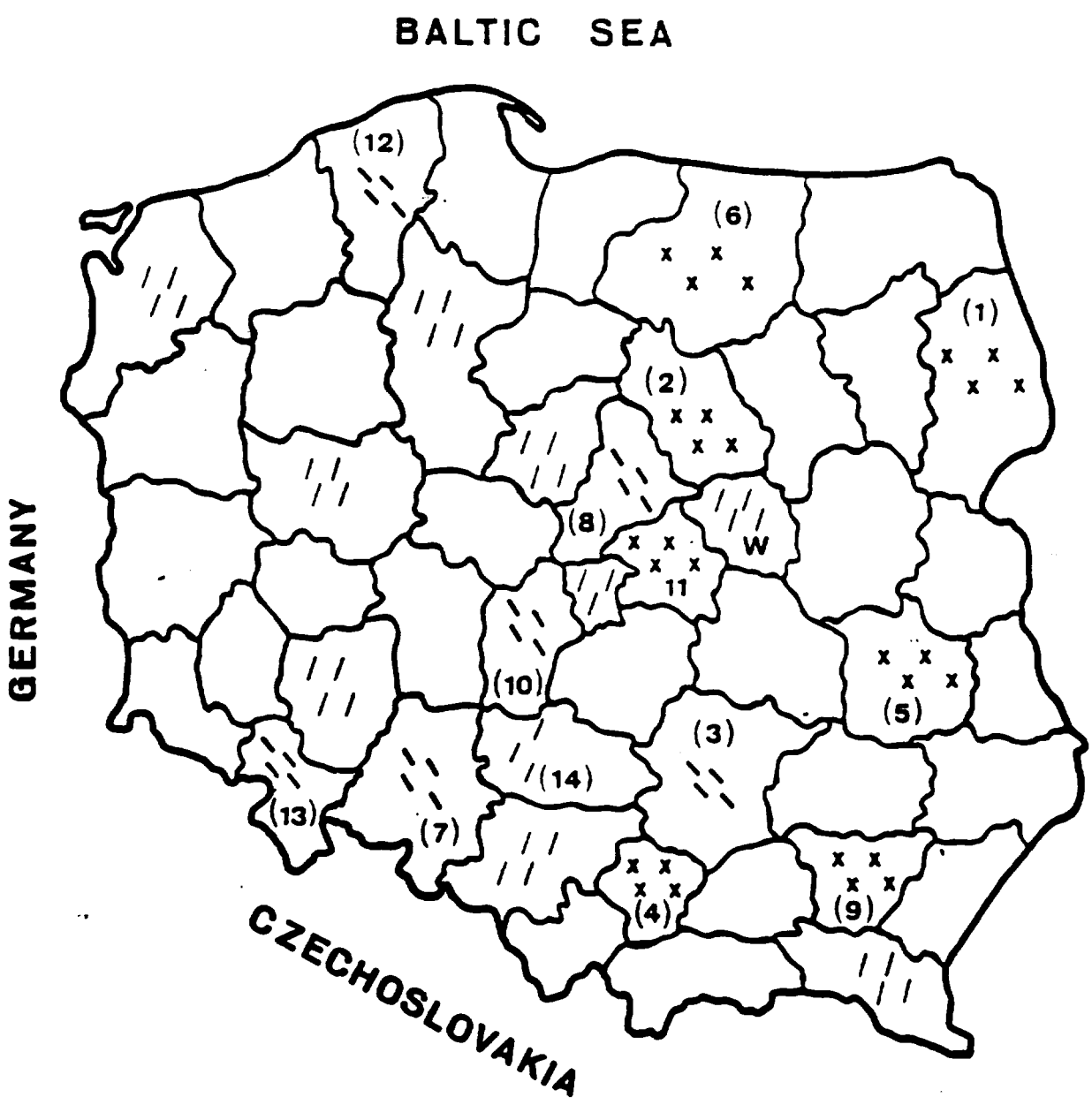

Figure 3 *Administrative districts of Poland. Studies performed on: daily diets (\); vegetables (/); daily diets and vegetables For numbering, see Figures 4 and 7.*

and 5 show large differences in lead intake as a function of location. The highest weekly intake values, which significantly exceeded the PTWI, were determined in the Walbrzych district (No.13 in Figure 4). In this district the mean lead intake by teenagers obtained in one year almost doubled the PTWI (Figure 4). This is a heavily polluted district. A worse situation occurred in the population of children (especially one year olds) which is illustrated in Figure 5. The mean lead intake was higher than JECFA PTWI for children in the majority of districts studied and the 90th percentile intake in all districts studied. The two PTWI values (Figure 5) were derived from a recalculation of the JECFA PTWI for children – 0.025 mg kg^{-1} body weight (WHO, Technical Report Series, 1987) based on body weight for 1 and 3 years old children.

Studies also included determination of the we mercury and cadmium intake. For mercury, weekly intakes less than 45% of PTWI, but relative intake of cadmiu Poland is even higher than lead (Figures 6 and 7). For cadm JECFA has not established separate PTWI for children levels (shown in Figure 6) were derived from adults PT 0.007 mg kg^{-1} body weight (WHO, Technical Report Se 1989), adjusting for body weight. Of particular concern i situation for children (Figure 6). The cadmium intake w this especially sensitive population is frequently higher thar of adults. In many regions, the average intake is also higher the calculated value of PTWI. Cadmium intake by teen (Figure 7) is also high, but not as dramatic as for children

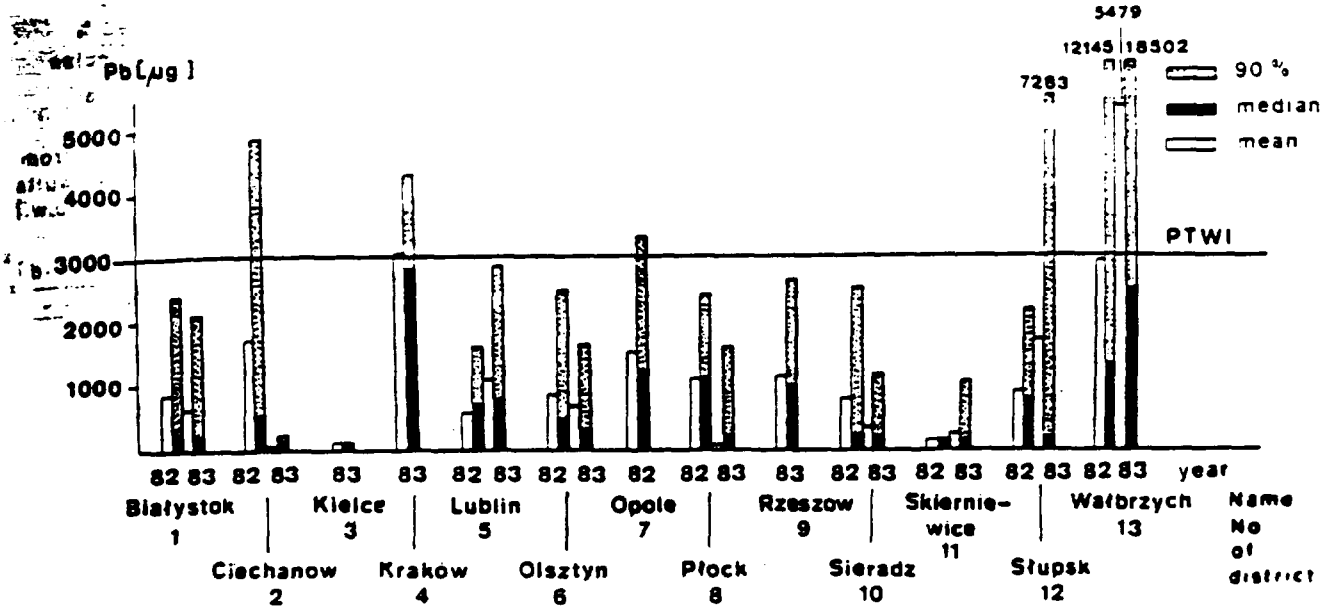

Figure 4 *Weekly intake of lead (µg) for teenagers 14–18 years old.*

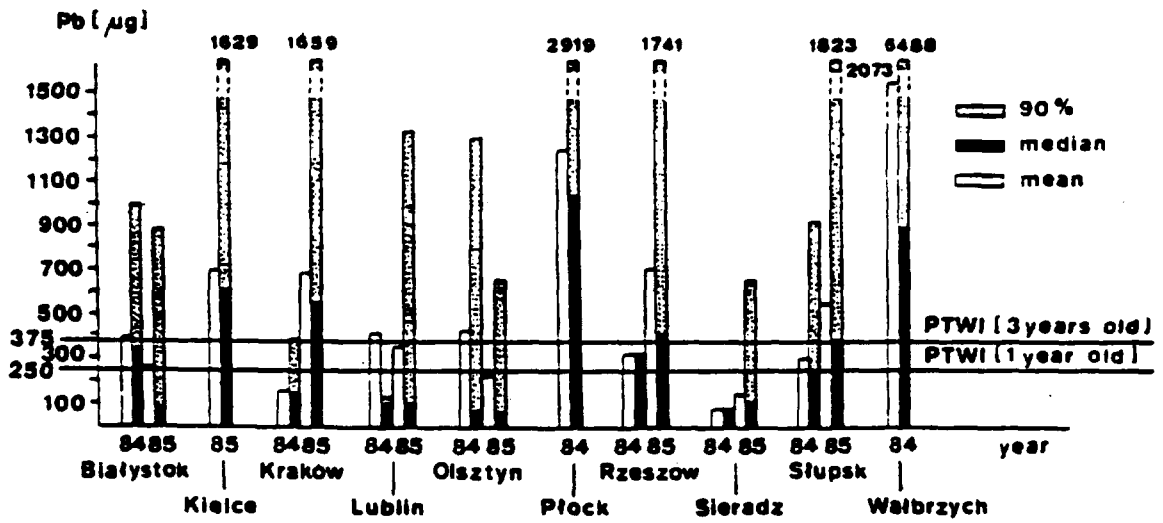

Figure 5 *Weekly intake of lead (µg) for children 1–3 years old.*

Lead and Cadmium Content in Vegetables

From 1986 until 1990, systematic monitoring studies were performed on the content of lead, cadmium, mercury, zinc and copper in selected, widely used Polish agriculture crops: vegetables (cultivated in fields and greenhouses), fruits and grains. Samples were collected in 18 districts at the farms in areas not directly exposed to metal pollution by industrial and mobile sources. Samples of ripe vegetables were taken using a random sampling technique with evenly spaced sampling sites consisting of greenhouses at 5–10 sites and open fields at 15–20 sites.

These studies had a goal of estimating a national background level of metals that could be used for evaluating the contamination of crops originated from industrial areas. The results are also used to determine permitted levels of contamination for Polish and international regulations.

The three-year study on vegetables was completed in 1988 (Zawadzka *et al.*, 1989, 1990). In one year, studies of vegetables were conducted with simultaneous monitoring of soil samples. Approximately 2,500 vegetable samples and 620 soil samples were examined. Currently, studies of fruits and grains are being conducted in Poland. So far about 400 samples of fruits and 350 samples of grains have been examined. The lead and cadmium contents in vegetables are shown in Tables 3 and 4.

The metal content was relatively low in the majority of the tested samples. However, in some samples higher than permitted levels of lead and cadmium were detected. Lead and cadmium content was high in carrots, garden beets, lettuce and parsley. The highest lead level was found in ground parsley leaves where about 20% of the samples exceeded 0.3 mg kg^{-1}. The 90th percentile lead contamination was also higher than 0.3 mg kg^{-1} in the case of carrots, parsley root, parsley leaves from the greenhouses, lettuce, ground cucumber and radishes in

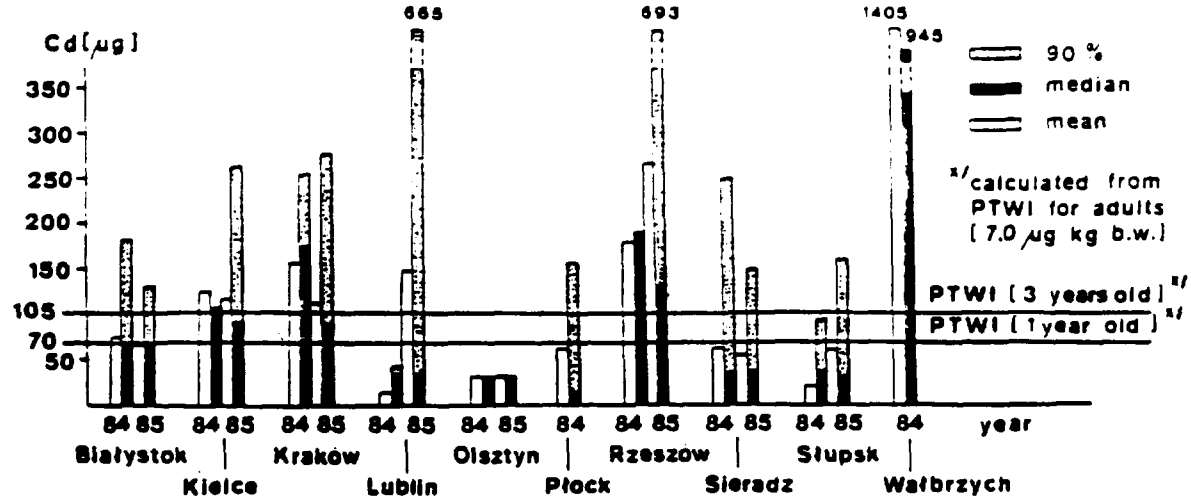

Figure 6 *Weekly intake of cadmium (µg) for children 1–3 years old.*

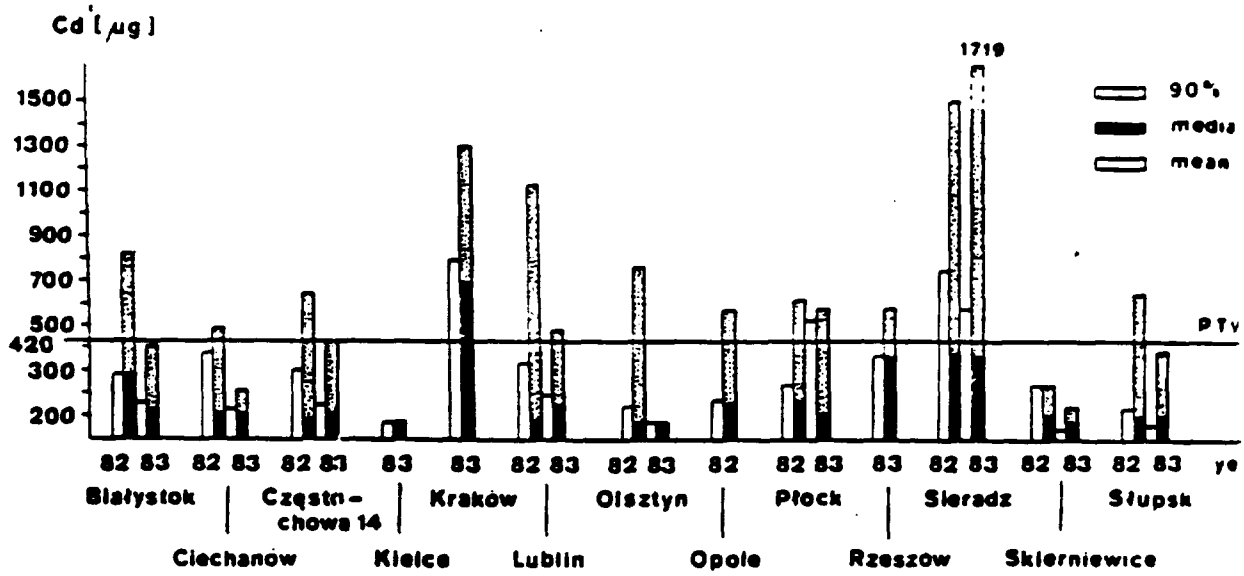

Figure 7 *Weekly intake of cadmium (µg) for teenagers 14–18 years old.*

certain years. The lowest lead content was measured for potatoes and tomatoes.

The highest content of cadmium was found in carrots for which over 30% of the samples exceeded 0.03 mg kg^{-1}. A slightly lower cadmium level was found in garden beets, ground parsley roots and leaves and ground and greenhouse lettuce (~25% exceeded 0.03 mg kg^{-1}). About 20% of the potatoes, which is a significant product in the daily diet in Poland, had cadmium content higher than 0.03 mg kg^{-1}. Greenhouse cucumbers had the lowest content of this metal.

The levels of these metals in fruits are much lower than in vegetables. High levels of cadmium were found in about 10% of the fruits studied mostly in the berry fruits: raspberries and strawberries. We believe the metal content to be relatively high for grains even though investigations are not completed. About 15% of the samples have had lead and cadmium content above 0.3 and 0.1 mg kg^{-1}, respectively. The most polluted grains with lead are buckwheat and rye and with cadmium are buckwheat, wheat and oats.

Since the samples were collected in areas remote f pollution sources the high lead and cadmium content in cer samples could be a result of the application of fertili containing excessive amounts of lead and cadmium. Phosp fertilizers were used in the majority of the places where cadmium content in vegetables and in soil was reported. L amounts of lead and cadmium are still contained in use Poland as fertilizers for agriculture industrial waste and sew sludge.

In some south-west industrial regions of Poland the and agricultural crops are so polluted that it is impossibl cultivate healthy vegetables and grains, especially for baby f production.

Sanitary Supervision Program in Poland

Since 1976, over 30,000 samples of food products from all regions of Poland have been tested for metals as a par Poland's Food Sanitary Supervision Program. The hig

Table 3 *Lead content in vegetables (mg kg^{-1}).*

Vegetable	Year	No. of samples	Median	Mean	90%	Min	Max
Potatoes	1986	70	0.068	0.092	0.240	<0.010	0.427
	1987	90	0.032	0.072	0.220	<0.010	0.565
	1988	90	0.040	0.068	0.120	<0.010	0.540
Cabbage	1986	48	0.008	0.111	0.250	<0.010	1.170
	1987	72	0.050	0.089	0.260	<0.010	0.516
	1988	66	0.023	0.126	0.320	<0.010	1.490
Carrots	1986	64	0.100	0.162	0.443	<0.010	0.780
	1987	125	0.062	0.102	0.280	<0.010	0.650
	1988	113	0.036	0.080	0.170	<0.010	0.760
Garden beets	1986	43	0.100	0.136	0.290	<0.010	1.192
	1987	83	0.071	0.094	0.220	<0.010	0.720
	1988	83	0.030	0.072	0.168	<0.010	0.400
Parsley root	1986	33	0.090	0.152	0.310	<0.010	0.460
	1987	65	0.087	0.148	0.325	<0.010	0.800
	1988	56	0.050	0.108	0.242	<0.010	1.085
Parsley leaves (field)	1986	34	0.190	0.290	0.718	0.020	2.877
	1987	54	0.130	0.380	0.450	<0.010	4.600
	1988	47	0.090	0.230	0.800	<0.010	1.462
Parsley leaves (greenhouse)	1986	10	–	0.238	–	0.080	0.370
	1987	31	0.200	0.218	0.430	<0.010	1.000
	1988	24	0.088	0.159	0.462	<0.010	0.790
Lettuce (field)	1986	14	0.150	0.300	0.387	<0.010	2.360
	1987	33	0.047	0.079	0.230	<0.010	0.270
	1988	29	0.050	0.129	0.300	<0.010	0.620
Lettuce (greenhouse)	1986	42	0.080	0.185	0.325	<0.010	2.370
	1987	99	0.066	0.132	0.300	<0.010	0.900
	1988	77	0.064	0.265	0.300	<0.010	1.880
Radish (field)	1986	9	–	0.088	–	<0.010	0.220
	1987	32	0.066	0.118	0.350	<0.010	1.620
	1988	19	0.020	0.065	0.260	<0.010	0.300
Radish (greenhouse)	1986	3	–	0.211	–	<0.010	0.473
	1987	27	0.042	0.089	0.173	<0.010	0.800
	1988	17	0.030	0.063	0.102	<0.010	0.397
Tomatoes (field)	1986	30	0.091	0.109	0.230	<0.010	0.420
	1987	53	0.027	0.057	0.180	<0.010	0.280
	1988	70	0.022	0.065	0.177	<0.010	0.865
Tomatoes (greenhouse)	1986	54	0.040	0.083	0.210	<0.010	0.540
	1987	100	0.030	0.077	0.184	<0.010	0.960
	1988	109	0.017	0.067	0.270	<0.010	0.800
Cucumbers (field)	1986	31	0.030	0.081	0.300	<0.010	0.300
	1987	42	0.037	0.070	0.270	<0.010	0.620
	1988	55	0.060	0.128	0.320	<0.010	0.460
Cucumbers (greenhouse)	1986	55	0.050	0.098	0.190	<0.010	1.580
	1987	96	0.025	0.055	0.120	<0.010	0.385
	1988	104	0.032	0.088	0.200	<0.010	1.580

Table 4 *Cadmium content in vegetables (mg kg^{-1}).*

Vegetable	Year	No. of samples	Median	Mean	90%	Min	Max
Potatoes	1986	70	0.006	0.010	0.020	<0.001	0.067
	1987	94	0.014	0.013	0.050	<0.001	0.080
	1988	90	0.010	0.018	0.060	<0.001	0.090
Cabbage	1986	48	0.004	0.007	0.019	<0.001	0.075
	1987	69	0.006	0.023	0.040	<0.001	0.659
	1988	66	0.003	0.009	0.040	<0.001	0.101
Carrots	1986	64	0.010	0.032	0.101	<0.001	0.323
	1987	128	0.031	0.045	0.145	<0.001	0.210
	1988	113	0.019	0.052	0.150	<0.001	0.480
Garden beets	1986	42	0.010	0.025	0.090	<0.001	0.136
	1987	81	0.019	0.037	0.150	<0.001	0.240
	1988	83	0.011	0.045	0.160	<0.001	0.790
Parsley root	1986	33	0.012	0.026	0.093	<0.001	0.138
	1987	63	0.011	0.036	0.140	<0.001	0.180
	1988	56	0.013	0.032	0.087	<0.001	0.180
Parsley leaves	1986	34	0.013	0.015	0.030	<0.001	0.064
(field)	1987	53	0.018	0.049	0.300	<0.001	0.480
	1988	47	0.011	0.046	0.110	<0.001	0.180
Parsley leaves	1986	10	-	0.013	-	0.001	0.023
(greenhouse)	1987	31	0.015	0.018	0.050	<0.001	0.084
	1988	23	0.012	0.012	0.021	<0.001	0.024
Lettuce	1986	14	0.016	0.024	0.047	<0.001	0.150
(field)	1987	33	0.021	0.031	0.109	<0.001	0.147
	1988	29	0.020	0.025	0.076	<0.001	0.100
Lettuce	1986	42	0.021	0.030	0.040	<0.001	0.370
(greenhouse)	1987	99	0.016	0.073	0.080	<0.001	0.590
	1988	76	0.019	0.026	0.070	<0.001	0.350
Radish	1986	9	-	0.010	-	0.003	0.028
(field)	1987	31	0.010	0.011	0.040	<0.001	0.050
	1988	19	0.002	0.027	0.030	<0.001	0.038
Radish	1986	3	-	0.010	-	0.003	0.020
(greenhouse)	1987	27	0.010	0.018	0.051	<0.001	0.075
	1988	17	0.008	0.011	0.035	<0.001	0.037
Tomatoes	1986	30	<0.001	0.007	0.020	<0.001	0.080
(field)	1987	52	0.006	0.006	0.009	<0.001	0.060
	1988	70	0.005	0.017	0.035	<0.001	0.410
Tomatoes	1986	56	<0.001	0.008	0.020	<0.001	0.040
(greenhouse)	1987	100	0.007	0.021	0.045	<0.001	0.350
	1988	108	0.006	0.011	0.030	<0.001	0.070
Cucumbers	1986	31	<0.001	0.004	0.010	<0.001	0.047
(field)	1987	42	0.004	0.010	0.026	<0.001	0.050
	1988	55	0.003	0.017	0.050	<0.001	0.100
Cucumbers	1986	59	0.005	0.006	0.015	<0.001	0.025
(greenhouse)	1987	96	0.006	0.010	0.024	<0.001	0.069
	1988	103	0.005	0.010	0.027	<0.001	0.090

values were detected in canned foods and in fruit and vegetable products. For example, during the last two years 6% of the samples of canned vegetable products have had lead content exceeding 0.6 mg kg^{-1}. In 1986, 10% of the jam samples were higher than 0.5 mg kg^{-1} and in 1988 about 15% of juice samples had lead content exceeding permitted levels. The majority of the results of these studies were published elsewhere (Nikonorow *et al.*, 1978; Zawadzka *et al.*, 1985, 1988) and the latest results are being prepared for publication.

Conclusions

Considering the average intake of lead and other metals in Poland, and also the average content of these metals in particular food products, we believe that the average intake of metals with food falls within tolerable doses. However, in industrial regions with extensive environmental pollution levels, the PTWI for children and adults and permitted levels in particular foodstuffs are frequently exceeded. This is especially important in the case of children (1–3 years old) and requires special attention and an immediate solution. We should also be aware that food is only one of the potential sources of contaminants intake, especially in areas of high environmental pollution.

The results presented here are mostly from studies coordinated and supervised by the National Institute of Hygiene. Similar studies have been done by other laboratories and research institutes in Poland, but the scope of these studies was usually limited to individual districts (Amarowicz *et al.*, 1985; Bulinski *et al.*, 1986, 1988; Chorazy *et al.*, 1987; Kucharski *et al.*, 1989; Nabrzyski and Gajewska, 1982, 1984; Olejnik *et al.*, 1985; Smoczynski *et al.*, 1984; Szymczak *et al.*, 1984; Zalewski *et al.*, 1989).

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Reductions in Dietary Lead Exposure in the United States

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Introduction

The United States Food and Drug Administration has made a concerted effort over the last two decades to reduce the exposure of the population to lead in foods (FDA, 1979). The agency has reduced lead exposure via the food supply by identifying and controlling sources of lead in foods.

The agency's primary efforts have been directed toward foods consumed by infants and children. This focus of the agency is due to the particular sensitivity of infants and children to the toxicity of lead. While many of the same sequelae of effects occur in both children and adults, those in children occur at lower levels of exposure. Infants and children are more susceptible, because (1) they consume more food per body mass, (2) they absorb lead more readily from the gastrointestinal tract than adults and (3) their major organs, such as the brain, kidneys and liver, are immature. The fetus also demonstrates an increased sensitivity to the effects of lead for the same reasons, and in addition, lead easily crosses the placenta. For this reason, the agency has devoted an appreciable portion of its recent efforts to minimize the dietary lead burden of women of child-bearing age.

Recent evidence indicates that lead toxicity in the young occurs at blood levels that were once thought not to be associated with the adverse effects of lead. Indeed, it is now clear that a threshold for lead has yet to be identified and will undoubtedly be established at a blood or body burden level which is below blood levels currently being reported in this country. Based on these recent developments and the deliberations of national and international health organizations, the Food Drug Administration (FDA) has continued in its efforts to reduce the dietary lead exposure of the population in the United States.

Lead is an ubiquitous, pervasive environmental contaminant. Figure 1 was adapted from the 1986 Environmental Protection Agency (EPA) air quality lead document by the Agency for Toxic Substances and Disease Registry (ATSDR) in its 1988 report on lead poisoning to Congress. It illustrates the variety of sources and pathways from which and by which lead enters the food supply. Food serves as a pathway of exposure to lead from many sources, including air, dust and water. Another major source of lead in food is from food processing, and until recently, the primary contributor from processing was from the use of lead solder in food cans. The blood lead concentration which serves as a primary index of exposure and toxicity reflects composite lead exposure from air, dust, soil, water and food. Ingestion of lead in foods can be one of the primary routes of lead absorption. In its 1988 report, the ATSDR estimated that approximately one million children in this country were at risk from lead in food.

Infant Foods

As stated previously, because of the particular [illegible] of infants and small children to lead, the early efforts of the agency in the 1970s to reduce dietary lead exposure focused on the use of lead soldered metal containers for infant food [illegible] (Jelinek, 1982). As shown in Table 1, the levels of lead in various infant food products have been substantially reduced. Indeed, the levels have been reduced by approximately 80–90%, so that the level is now down to an average of about 0.01 μg g^{-1} or 10 ppb. These reductions were realized through a cooperative effort with the infant food manufacturers and were achieved in large part by the decision of industry to switch from cans to glass to package infant foods. Other means included the shift of infant formula production to welded three-piece cans or drawn two-piece steel cans and the careful selection of raw materials and exclusion of contamination during handling and processing.

In its 1986 document, *Air Quality Criteria for Lead*, the EPA estimated that for a 2-year old child, approximately 47% of the baseline lead exposure came from food, excluding the contribution from water. The remainder of the lead exposure was from air, dust, water and soil. This is depicted in the pie chart on the left in Figure 2. The EPA estimated that the bulk of lead in food originated from direct air deposition (45%) and the use of lead-soldered food cans (42%). The data cited in the 1986 EPA report gave a fairly accurate portrayal of lead exposure for children in the early part of the 1980s. This is particularly the case for dietary lead, because the analysis relied on data that were obtained by the FDA as part of its Total Diet Study (TDS) from the early 1980s. Since that time there has been a considerable decrease in the overall dietary exposure to lead. As shown in the right hand pie chart in this figure, the current baseline dietary exposure for a 2-year old child is estimated by the Food and Drug Administration to comprise approximately 16% of the total exposure. This analysis is based on the use of the last complete market basket from the TDS and a recent review of the national ambient air quality standards for lead by the EPA (EPA, 1989).

Figure 3 is a pie chart which depicts the current estimation by the Food and Drug Administration of the baseline lead

† *Special issue incorporating the Proceedings of of the Symposium on the Bioavailability and Dietary Exposure of Lead.*

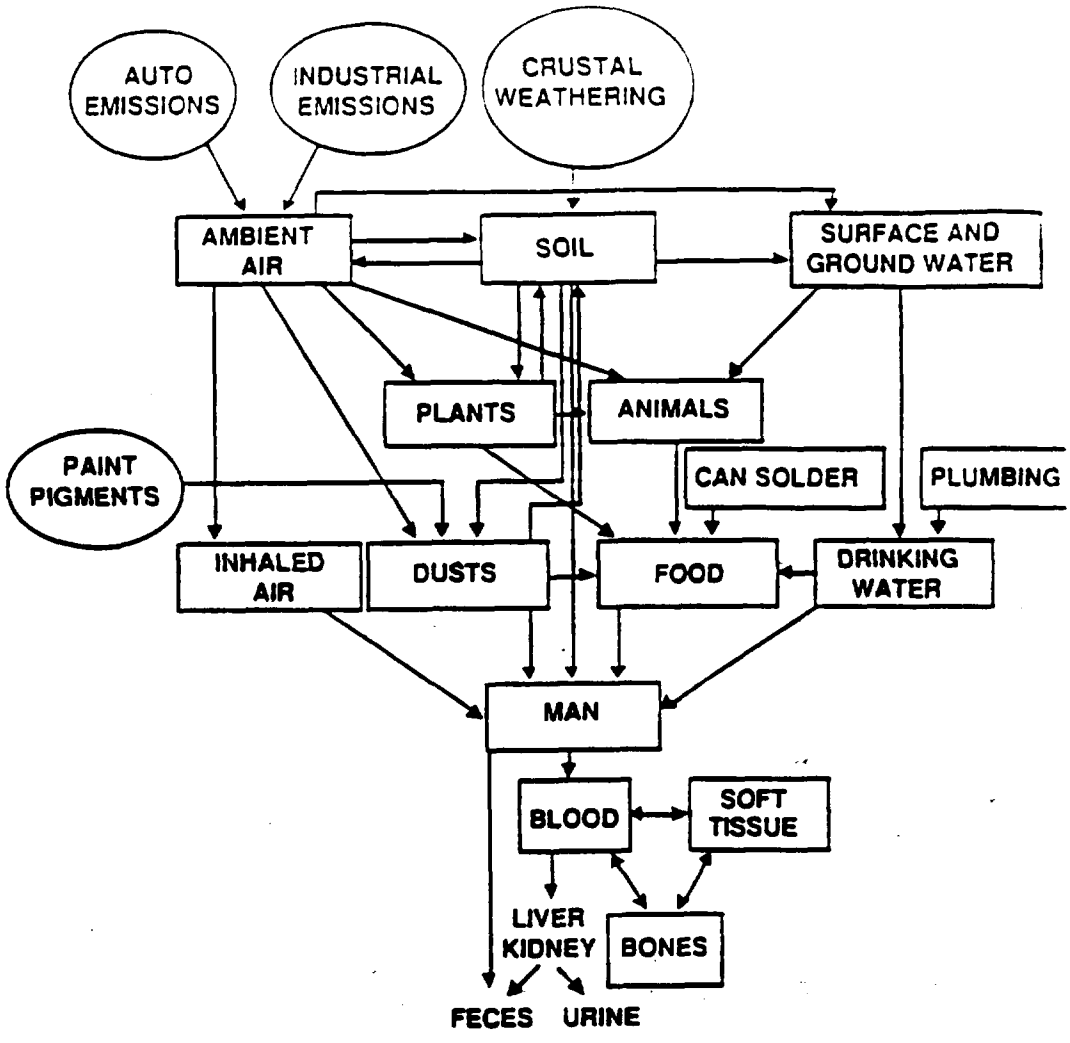

Figure 1 *Pathways of lead from the environment to man, and body disposition of lead (EPA, 1986).*

exposure of women of child bearing age. According to this estimation, dietary lead comprises approximately 43% of the total baseline lead exposure. In its 1986 air lead document the EPA estimated that dietary lead, excluding the contribution from water, comprised about 77% of the total baseline lead exposure for this age group. Therefore, as was shown previously for children, there has been an appreciable decrease in dietary lead exposure for women of child-bearing age in this country. These reductions in dietary lead have been measured in the FDA's Total Diet Study and is undoubtedly due in part to the concomitant decrease in the use of lead solder in food cans.

Table 1 *Lead levels in infant foods* ($\mu g\ Pb\ g^{-1}$).

Product	Early 1970s	Late 1980s
Infant formula	0.10	0.010
Infant juices	0.30	0.011
Infant foods	0.15	0.013
Evaporated milk	0.52	0.010

Total Diet Study

The Total Diet Study (TDS), which includes a roun for lead in market basket samples, is the agency's ann basket survey (Pennington and Gunderson, 1987). I the agency with baseline information on the levels of of pesticide residues, nutrient elements and envi contaminants, like lead, in the diet. The study is p useful in identifying trends in the levels of a contam lead in the food supply and assists in signaling poten health problems. The survey involves the purchase, p and analysis of typically consumed foods. The TDS United States national dietary survey which ass exposure to dietary lead of a number of age groups, infants, children and women of child-bearing age.

Figure 4 depicts the annual results from the TDS lead exposure for adolescent males. The data on di exposure for adolescent males is important not bc segment of the population is of particular concern, b this population group has the longest continuous rec dietary lead in the TDS. It is most useful for demons reductions in dietary lead that have occurred ove decade. Until 1980 there was no demonstrable change

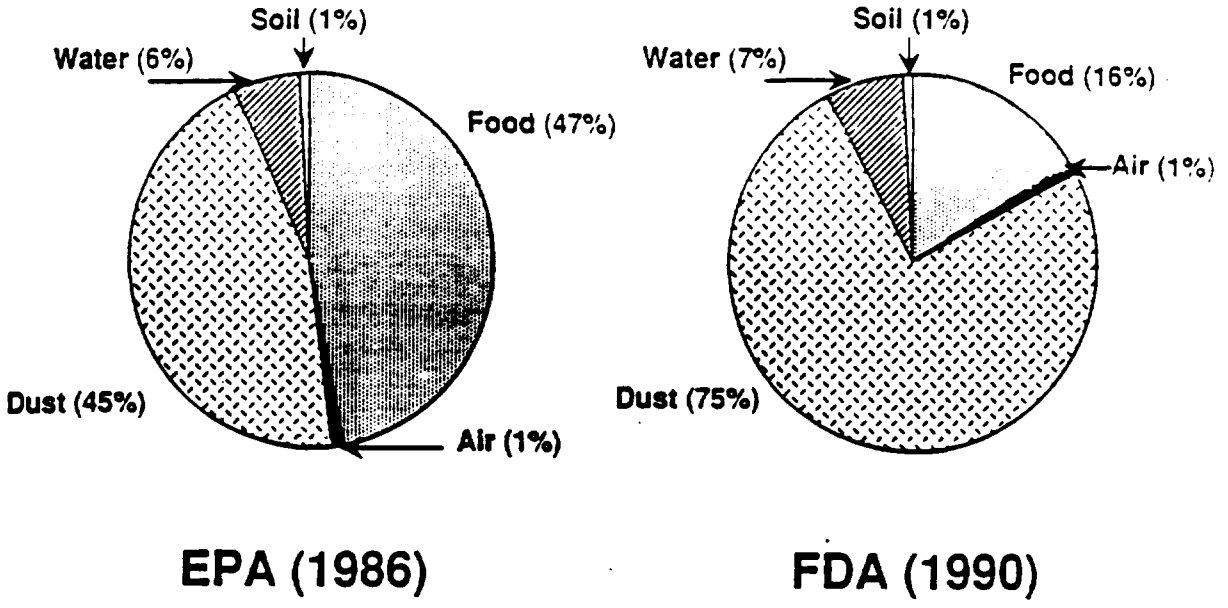

Figure 2 *Lead exposure for 2-year old children.*

lead exposure for this group. From 1980 until the present there has been a sizable decrease in dietary lead exposure in this group, on the order of approximately 88%, down from 84 $\mu g\ day^{-1}$ in 1980 to 10 $\mu g\ day^{-1}$ in 1988.

Similar reductions in dietary lead are noted in Figures 5 and 6 which deal with infants, young children or toddlers and women of three different age groups. Infants are defined in the TDS as being from 6 to 11 months of age, while toddlers are defined as 2 years of age. As with the adolescent males, dietary lead did not start to decrease until about 1980 for these age groups. Indeed, it would appear that dietary lead actually increased during the latter part of the 1970s. The percentage reductions for each group was about as great as that for adolescent males, and in absolute terms was reduced from between 34 to 44 $\mu g\ day^{-1}$ in 1980 to 5 $\mu g\ day^{-1}$ by 1988.

Figure 6 presents data from the TDS that demonstrates the dietary reductions that have occurred in the three female age groups. These three groups are defined as 14 to 16-year old, 25 to 30-year old and 60 to 65-year old. In 1984 the dietary lead content varied from approximately 27 to 30 $\mu g\ day^{-1}$, and by 1988 the levels were 7 to 9 $\mu g\ day^{-1}$, and were on the order of about 25% of 1984 levels. While these reductions are not of the same magnitude as those seen with the previous age groups they are consistent in that the reduction was sizeable. It must be noted that no values are presented for years before 1984 for women, because before 1982, the TDS did not include these groups. When the TDS was revised in 1982, these three age groups for women were included. If these groups had been included in the old TDS, the reductions in their dietary lead levels would undoubtedly have been of the same magnitude as seen with the other age groups, on the order of 80%.

The latest (1989–1990), preliminary information from the FDA TDS indicates that the reductions in dietary lead have either leveled off or have continued, although at a lower rate, and now range from 5 to 11 $\mu g\ day^{-1}$. These data indicate that the greatest reductions in dietary lead have occurred during the last decade, undoubtedly to the reduced use of lead solder in food cans and leaded gasoline. Further reductions will be smaller and much more difficult to achieve. The data also indicate that we have reached the limits of quantitation in the TDS.

The analytical methodology (graphite furnace–atomic absorption spectrometry) currently used in the TDS has a quantitation limit of 20 ppb. Approximately 85% of the samples in the study today do not have quantifiable levels of lead. If the concentration of lead in a sample is below the quantitation limit, but still above zero, this estimated level is used in the calculation of the dietary lead intake. Those samples in which no lead is detected are reported as zero which in turn is used in

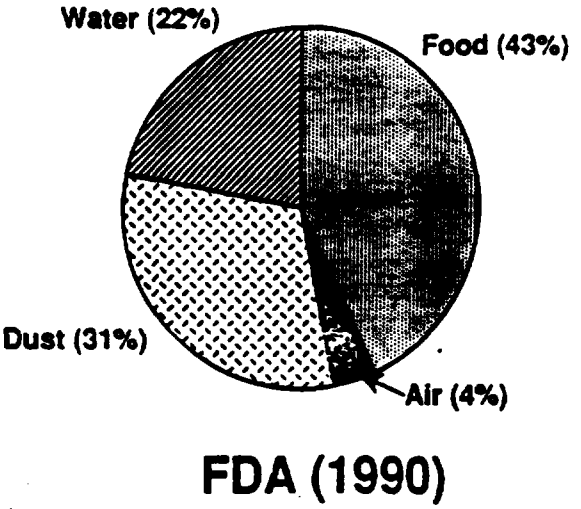

Figure 3 *Sources of lead exposure. Females, child-bearing age.*

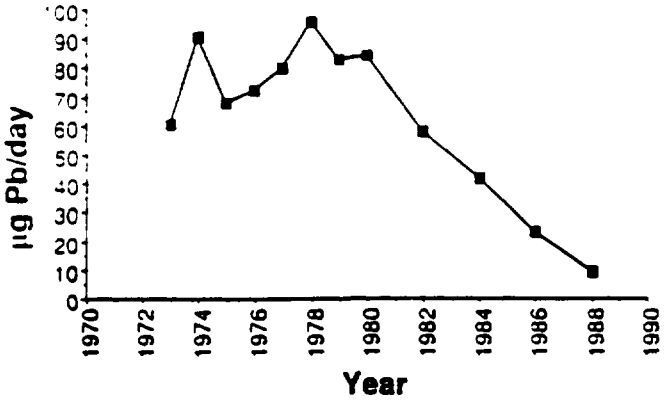

Figure 4 *Lead intake for adolescent males from FDA Total Diet Study.*

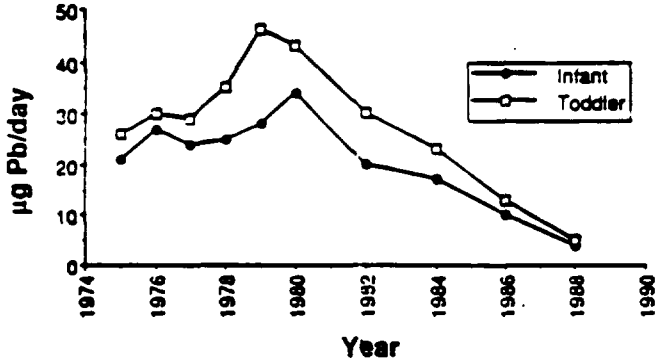

Figure 5 *Lead intake for infants and toddlers from FDA Total Diet Study.*

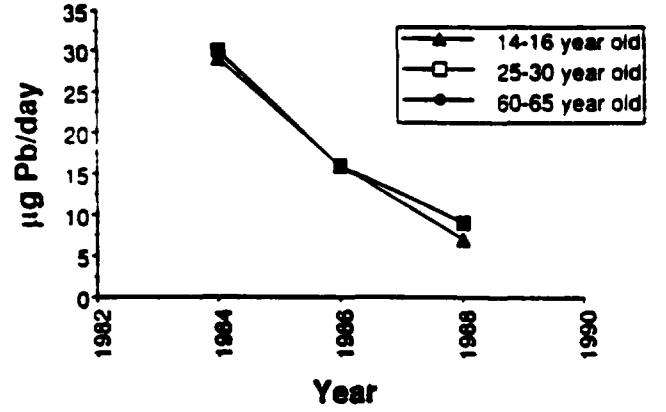

Figure 6 *Lead intake for females from FDA Total Diet Study.*

the calculation of dietary lead intake. To quantify these lower levels of lead and to measure further reductions in dietary lead a lower level of quantitation is required (Capar, 1991).

The lack of reductions in dietary lead in the 1970s for any of these age groups is in contrast to the considerable reductions in the use of leaded gasoline and blood lead levels that were realized during this same period of time (Amnest, 1983). This suggests that a factor other than air lead resulting from the use of leaded gasoline was primarily responsible for the reductions in dietary lead noted in the TDS. That factor was undoubtedly the reduction in the use of lead solder in food cans.

Lead Solder

The major food processing source of lead, as well as one major sources of lead in food, arises from the use of lead in food cans. Estimates by the FDA and others contribution of lead solder from food cans to the dietary burden have ranged from 14 to 45% (FDA, 1979; EPA, These data clearly indicate that there is appreciable mig of lead from the solder to the food. The effort to elimina use of lead solder in what we will call adult canned food initiated by the domestic canning industry in 1979, as seen Figure 7. All of the data displayed in this figure an next figure was supplied by the Can Manufacturers Institu that time, approximately 90% of domestically produced used lead solder. Presently, approximately 3.8% of dom food cans are made with lead solder and this will continu rapidly decrease over the next year. The use of lead solde soft drink cans was fairly low in 1979, on the order of 10% by 1982 had been entirely discontinued.

Figure 8 depicts the same data in the previous figure presents it in numbers of cans. The major point of this figure that while the percentage of food cans using lead solder w low, there were still about a billion domestically produced cans that used lead solder in 1989. This figure also shows domestically produced lead soldered cans have been gradu replaced by drawn/redrawn two-piece and welded three-piece cans.

In terms of imported cans, unfortunately there is very no information available on the number of cans imported int United States and the prevalence of the use of lead solder FDA is investigating the issue in an attempt to quantify the of lead solder in imported food cans.

Survey of Adult Canned Foods Eaten by Small Children

As infants gradually switch from infant food products, they s to consume adult-type foods which include foods consumed cans. The agency recently conducted a survey of lead in cann foods eaten by young children as part of its ongoing effort identify the sources of dietary lead in this sensitive segment the population (Capar, 1900). Ten foods commonly eaten fairly large amounts by children were included in the surv As can be seen in Figure 9, there are appreciable differences the lead content between those foods packaged in cans with without lead solder. The difference is approximately five fo 0.21 µg Pb g^{-1} of food in lead soldered cans *versus* 0.04 µg in non-soldered cans.

Lead Glazed Ceramics

The agency has recently proposed establishing new regulat standards for lead in ceramic pitchers (FDA, 1989). T proposal also includes initiatives for other types of ceram foodware. These proposals have been made, based on evidenc of lead migration from lead glazes to food storage, particula under acidic conditions. Indeed, this migration of lead from glaze can be substantial, and cases of lead intoxication ha been reported in the literature. According to a recent estim by the agency, the upper bound lead exposures at a 0.1 mg l level of lead migration into acidic beverages stored in ceram pitchers are 15 and 17 µg per person day^{-1} for infants

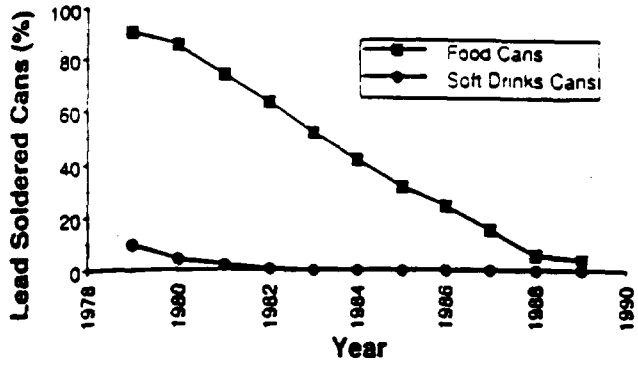

Figure 7 *Percent lead soldered cans of total cans shipped (United States) (CMI, 1990).*

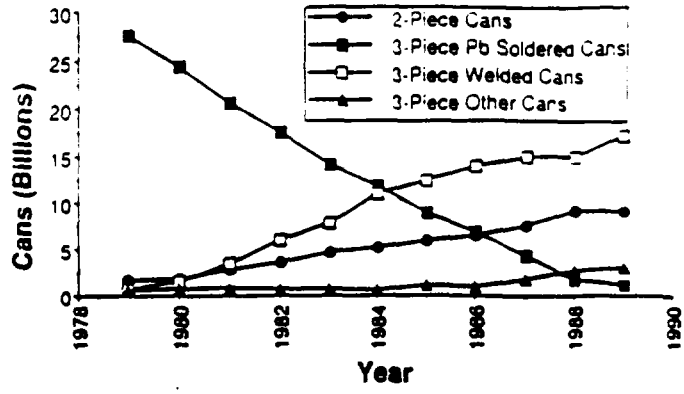

Figure 8 *Types of food cans shipped (United States) (CMI, 1990).*

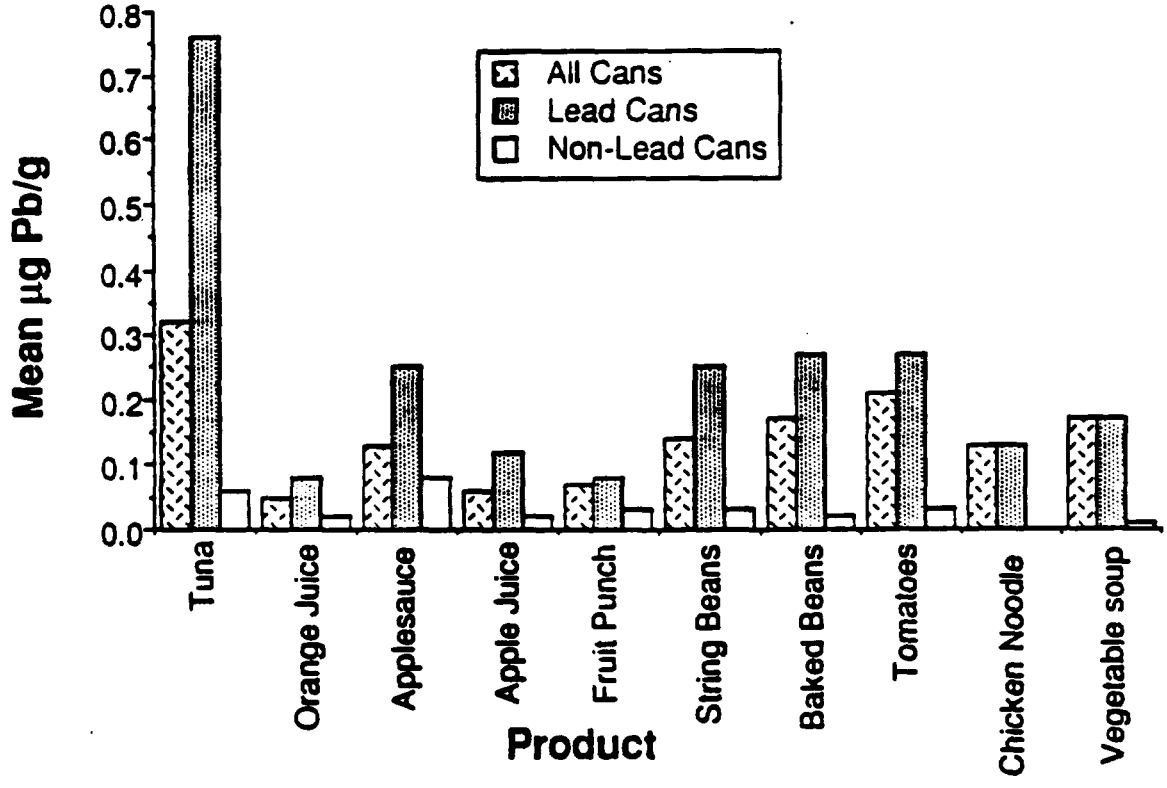

Figure 9 *Lead levels in canned foods. FDA canned food survey F 1982I83I84I85 (Capar, 1990).*

toddlers, respectively. These represent considerable contributions to the dietary lead burden when one considers that, as was noted previously, the current dietary exposure from the TDS is on the order of 5 µg day^{-1} for these age groups. The proposal to establish a new standard for ceramic pitchers was made, because it was considered likely that acidic fruit-based beverages, which are consumed frequently and in large amounts by children, would be stored in ceramic pitchers. Furthermore, large numbers of ceramic pitchers with lead glazes are sold in this country and could be used in this manner, and therefore, the number of children at risk is potentially quite large.

Because of the dynamic nature of the lead problem (*e.g.*, lower adverse effect levels in human populations and reductions in specific sources), the agency is currently reassessing the extent of the lead problem in foods. This analysis involves a determination of the contribution of dietary lead to the total body burden of lead and the development of a program for lead in foods that encompasses the identification and quantification

of specific sources of lead in the diet. These sources would include lead capsules used on wine bottles, dietary supplements such as calcium supplements, bottled water and food additives. Along with the identification of dietary lead sources, there is an absolute need to improve the analytical methods for monitoring lead in foods.

Conclusions

In conclusion, the following are the major points that can be made in regard to dietary lead exposure in the United States.

- Major reductions in the lead content in infant foods were achieved in the 1970s by switching to glass packaging.
- In the 1980s, the FDA Total Diet Study documented reductions in dietary lead of approximately 80 %.
- The reductions of lead in adult foods were achieved in large part by the discontinuance of lead solder in food cans.
- The reductions in lead exposure by removing the more obvious sources of lead in the diet have been achieved. Further reductions will be more difficult to identify and effect.
- There will be more emphasis on the dietary lead exposure of specific populations (*e.g.* consumers of ethnic foods).

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FDA Total Diet Study: Dietary Intakes of Lead and Other Chemicals

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Abstract

The history of the Food and Drug Administration's (FDA's) Total Diet Study (TDS) is described, together with some details on how it currently functions to monitor levels of lead and other chemicals in the US diet. Along with the history and structure of the TDS, a brief description of our recent effort to combine TDS lead data with data from the USDA food consumption database in a user-friendly report-generating computer program will be presented. This system will help us to produce lead exposure updates almost immediately when new analytical results are added to the TDS database.

The FDA has been working to reduce lead exposure to populations particularly susceptible to the toxic effects of this metal, namely, children and women of childbearing age. Our efforts in this area presently include establishing specifications for lead in foods and food additives; controlling the amount of lead in such items as canned food, bottled water, dietary supplements and wine; and controlling lead exposure from the use of ceramic pitchers, dinnerware and decorated glass. We are working to educate consumers to the dangers of exposure to lead and the means to avoid this exposure, and we are actively working with industry and consumer groups to monitor and reduce dietary intake of lead.

Lead exposure may occur by several different pathways. These pathways are summarized in Figure 1, which shows the sources of lead exposure for children and young women. In toddlers, food accounts for about 16% of their total lead exposure, while in young women, food accounts for about 43% of total lead exposure (FDA estimate). The importance of reducing lead exposure from food sources for both of these populations cannot be overemphasized. The TDS is a tool used by the FDA to monitor and estimate lead exposure in the US diet (Pennington, 1983).

The primary purposes of the TDS are to determine the dietary intakes of pesticide residues, heavy metals, industrial chemicals, essential minerals and radionuclides, and to compare the intakes of these substances with Acceptable Daily Intakes, Recommended Dietary Allowances, or Estimated Safe and Adequate Daily Dietary Intakes (Pennington and Gunderson, 1987). In addition, the TDS allows identification of trends: it may identify isolated contamination sources, and it serves as a final check on the effectiveness of pertinent US regulations and initiatives.

The FDA initiated the TDS in May 1961, primarily in response to concern about levels of radioactive contamination in foods from atmospheric nuclear testing (Lombardo, 1986). At that time there was no nationwide government-sponsored program designed to estimate dietary intake of radioactive materials. The first TDS estimated levels of strontium-90 and cesium-137, as well as organochlorine pesticide residues, organophosphorus pesticide residues and selected nutrients in the diets of young men. The TDS has been ongoing since 1961, with considerable modification and expansion since its beginning.

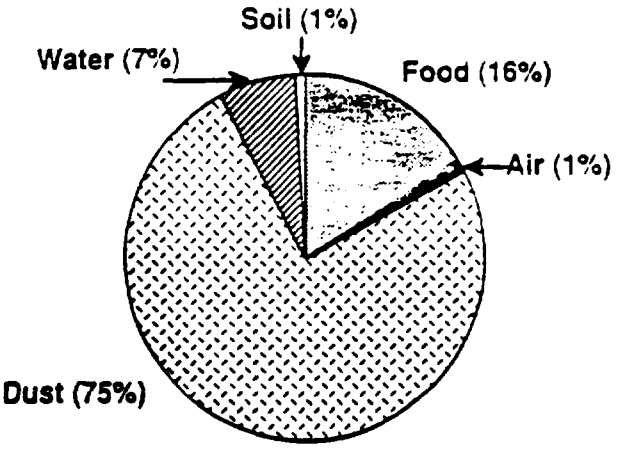
The diets for the various age-sex groups, along with caloric content, used in the TDS from its inception to mid-1982, are shown in Figure 2 (Pennington and Gunderson, 1987). Food consumption data from the US Department of Agriculture's (USDA's) 1955 Household Food Consumption Survey were used to develop the first TDS diet. This diet was based on quantities of foods from 11, and later 12, food commodity groups, such as dairy products, grains, vegetables, and so forth, as suggested for males 16 to 19 years old in USDA's moderate cost food plan. This diet followed the general nutritional plan of moderate income families, but was somewhat modified to meet nutritional goals. It was excessive in energy intake, providing about 4,200 kcal day^{-1}, to allow assessment of maximum exposure to dietary contaminants.

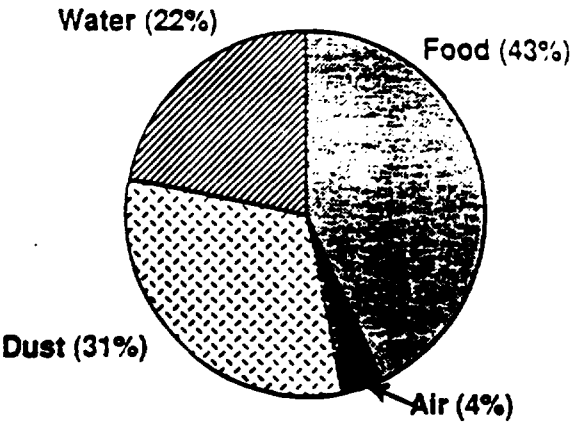
Collected foods were assembled by commodity type, samples were prepared for consumption, composited and analyzed.

This same diet was used between 1962 and 1970 with adjustments for regional food patterns. In 1975, assessments of infant's and toddler's diets were initiated. In 1982, the current TDS diet was initiated.

Selection of the current diet was based on two nationwide surveys covering about 50,000 people, the 1977-78 USDA National Food Consumption Survey and the 1976-80 National Health and Nutrition Examination Survey (NHANES II). About

[a] As reported to the FDA by the Can Manufacturers' Institute, March 1990.





Children, 2 yrs old **Females, Child-Bearing A**

Figure 1 *Sources of lead exposure for selected populations expressed as a percentage of total exposure (US EPA, 1*

5,000 different foods were identified in these two surveys. Practical considerations precluded the collection and analysis of all the approximately 900 foods that represent 95% by weight of the US diet, or even the 500 foods required for 90% representation. An aggregation scheme was used by the FDA to select 234 foods to represent the 5,000 foods in the USDA database. Most of the individual foods selected represented a group of foods similar in type and nutrient content; the selected food is the one food in the group that is consumed in the greatest amount. For example, apple pie represents dozens of different fruit pies and pastries containing fruit, and a number of pasta dishes are represented by spaghetti and meatballs in tomato sauce. Thus, the 234 selected foods can be said to represent all 5,000 foods identified in the two surveys (Pennington, 1983).

The end result of this extensive revision to the TDS was a set of updated, nationally representative diets for eight distinct age-sex groups (Figure 3) from infants to mature adults, including males and females. Individual foods were analyzed, rather than the food group composites of older TDS studies.

The current collection and analysis scheme for the TDS is shown schematically in Figure 4. Foods for the TDS program are collected by inspectors from FDA District offices. The technique of collecting representative foods is another aspect of the TDS that has changed considerably over the years. For the first 20 years of the TDS, market baskets of foods were purchased approximately 30 times annually from grocery stores by FDA District offices in the south, east, central and western USA, and the foods were prepared for consumption by cooking or other methods. The prepared foods were then separated into the 12 commodity groups of like foods that were mentioned previously, and the foods in each group were blended in amounts proportional to their weights in the diet of a typical teenage male. The composites representing the 12 commodity groups were then analyzed.

Under the 1982 TDS revision, foods are collected once a year from retail stores in each of the four geographical areas of the USA, giving a total of four collections. Each collection, or 'market basket' as it is known, consists of identical foods purchased from grocery stores in three cities within the geographical area. Collections by geographic areas are r For example, the northeast collection may take place spring of one year and in the fall of the next. The cities each geographic area are changed with each collection. two-thirds of the foods collected are adult foods, and on represent infant and toddler foods. The same surrogate are always chosen. No brand names are specified; t selection is random. Because each city is in a differen District, the year's collections involve all 12 FDA D TDS collections have been made from all states except

Foods collected by the District Offices are ser centralized location where the three samples of a food fr

YEARS USED	AGE-SEX GROUPS	CALORIC CON KCAL DA
1961-62	YOUNG MALE	4200
1962-70	YOUNG MALE	4200
1971-74	YOUNG MALE	3900
1975-82	YOUNG MALE	3900
	INFANT	880
	TODDLER	1300

Figure 2 *FDA Total Diet Study populations evaluated inception of the study to 1982.*

- 6 - 11 MONTHS OLD
- 2 YEARS OLD
- 14 - 16 YEAR OLD, MALE AND FEMALE
- 25 - 30 YEAR OLD, MALE AND FEMALE
- 60 - 65 YEAR OLD, MALE AND FEMALE

Figure 3 *FDA Total Diet Study population groups.*

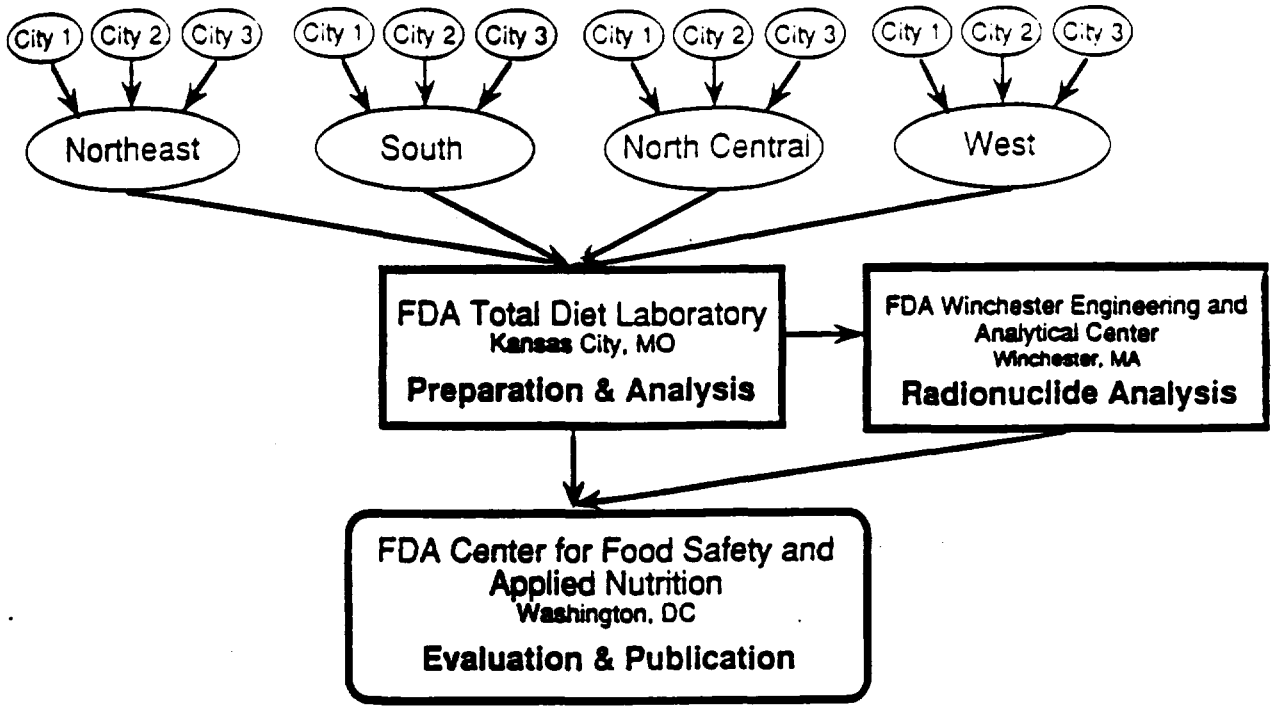


Figure 4 *Schematic depiction of collection, preparation and analysis of FDA Total Diet Study foods.*

three cities are combined and prepared table-ready under standardized and carefully controlled conditions. Analyses are carried out at the FDA Total Diet Laboratory in Kansas City. Radionuclide analyses are performed at the FDA's Winchester Engineering Analytical Center in Winchester, MA. Analytical data are returned to the FDA's Center for Food Safety and Applied Nutrition (CFSAN) in Washington, DC, for evaluation and publication.

Analytes have been and may be added to the TDS according to the needs and concerns of the FDA. Figure 5 shows a few substances that have been of continuing interest over the years, along with the year when each was added to the analysis list. Presently, nearly 300 chemicals are analyzed for by FDA chemists.

Analytical methodologies for organohalogen, organophosphorus and other pesticides and organic contaminants have been modified or changed to reflect new developments in analytical chemistry. Because foods purchased at retail and prepared ready-to-eat generally are expected to contain very low levels of contaminants, the analytical methods used to analyze TDS foods have been modified to permit quantitation at levels 5 to 10 times lower than those commonly found in FDA enforcement monitoring.

Techniques for determining lead have also changed over the years. Lead content was originally determined by atomic absorption spectrometry. Currently, dry-ash digestion followed by graphite furnace atomic absorption spectrometry is used for this analysis. The method has a lead quantitation limit of 0.02 $\mu g\ g^{-1}$, or 20 ppb (Capar, 1991).

Results of the TDS analyses have been published in the scientific literature since the inception of the study:

As was previously noted, nearly 300 pesticides, pesticide metabolites and alteration products, industrial chemicals, nutrients and other substances are monitored in the TDS (Lombardo, 1989). Calculated dietary intake levels of pesticides have generally been less than 1% of the acceptable daily intakes (ADIs) established by the expert committees of the World Health Organization and the Food and Agriculture Organization of the United Nations. However, in the 1960s it was found through the TDS that for the persistent organochlorine pesticide dieldrin, the intake was close to the ADI. Use of dieldrin was revoked and the TDS has monitored its steady decline in the diet since that time.

In the 1971 TDS, polychlorinated biphenyl (PCB) residues were found in a ready-to-eat breakfast cereal. Follow-up investigations revealed that the chemical had migrated from the paperboard package that had been produced from PCB-contaminated recycled paper. This finding ultimately lead to a regulation limiting the PCB content of paper intended for food-contact use.

In 1975, residues of the fungicide and preservative pentachlorophenol were found in unflavored gelatin.

SUBSTANCE	YEARS ANALYZED
ORGANOHALOGEN PESTICIDES	1961-PRESENT
POLYCHLORINATED BIPHENYLS	1971-PRESENT
ORGANOPHOSPHORUS PESTICIDES	1961-PRESENT
PENTACHLOROPHENOL	1961-PRESENT
ARSENIC	1964-PRESENT
LEAD	1973-PRESENT
TOTAL NUMBER OF ANALYTES > 300	

Figure 5 *Selected analytes determined in the FDA Total Diet Study.*

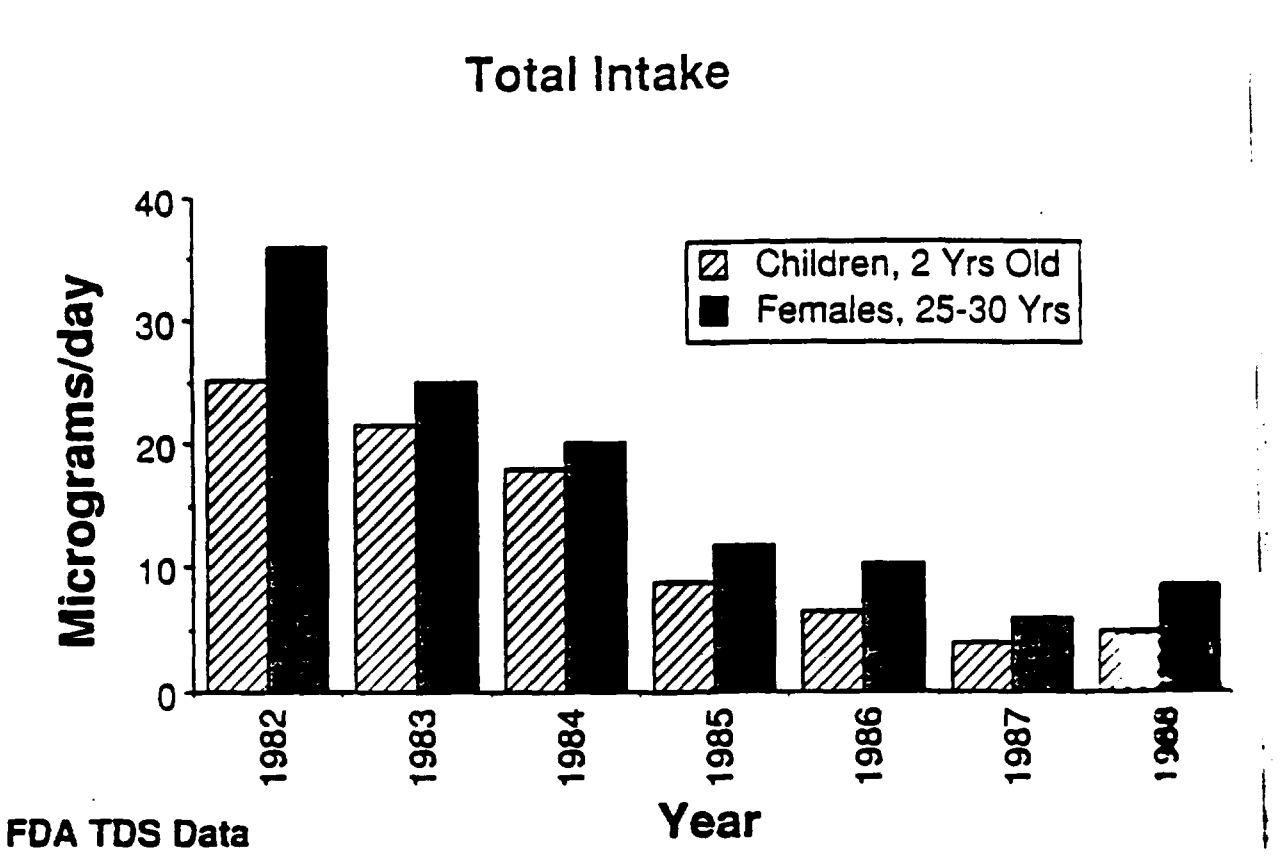


Figure 6 *Trends in dietary lead intake for children and women of childbearing age, from 1982 to [illegible]*

Pentachlorophenol had been used to treat hides in slaughterhouses, and many of these hides were shipped to gelatin manufacturers. The use of pentachlorophenol had been discontinued several years before by US processors. Investigation revealed that the gelatin tested was a mixture of both domestic and Mexican gelatin. The Mexican gelatin was found to contain pentachlorophenol and was not permitted to be used in food.

For nutritional elements, one notable observation was that of high levels of iodine in the US diet. Intake levels have ranged from about 2 to over 10 times the Recommended Dietary Allowances for this element. Through the TDS, major sources of iodine have been identified as dairy and grain products, and foods containing the food color FD&C Red No. 3

The TDS has been very useful in monitoring the overall level of lead in the US diet. As seen in Figure 6, lead intake has steadily declined over the last decade from about 36 $\mu g\ day^{-1}$ for adult females to about 8 $\mu g\ day^{-1}$ today. For toddlers, the levels declined from about 25 μg day12 to the current level of about 5 $\mu g\ day^{-1}$.

In the past, the major source of dietary lead was lead solder used in food cans. Since 1979, domestic can manufacturers have voluntarily discontinued most uses of lead-soldered cans in domestic food packaging (Figure 7). As a result, in 1990 only about 3.5% of all food cans produced in the US have lead-solder construction.* The quantity of lead-soldered cans reaching the US from foreign sources is not known. Recently, the FDA began a survey of foreign governments to ascertain the [illegible] lead-soldered cans overseas.

Figure 8 illustrates the decline in lead levels [illegible] canned foods over the last six years. The 1989 lead [illegible] canned foods is only about 10% of the 1982 level. This [illegible] will continue to drop as remaining lead-soldered [illegible]

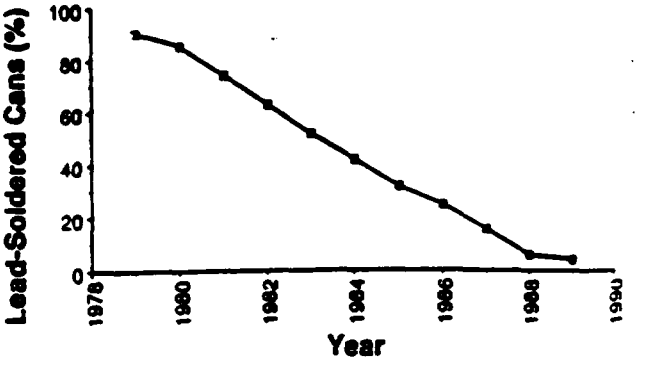


Figure 7 *Percentage of domestic food cans that are of lead-solder construction.*

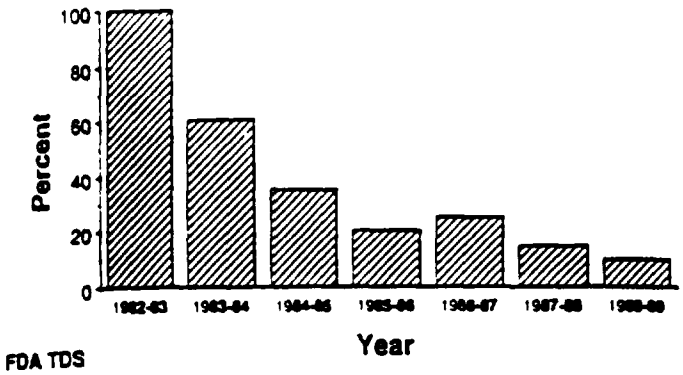


Figure 8 *Lead in domestic canned foods expressed as a percentage of 1982–83 lead level in canned food.*

removed from the market.

We are facing the difficulty that lead levels are becoming so low that current analytical methods will be inadequate to determine them. For example, as mentioned previously, the TDS lead quantitation limit is 0.02 $\mu g\ g^{-1}$, or 20 ppb. In the case of infants, the FDA uses a tolerable range for lead intake of about 6 to 10 $\mu g\ day^{-1}$ for a 10-kg child. To ascertain whether lead intakes from foods are near this 10 $\mu g\ day^{-1}$ level, a quantitation limit of about 5 $\mu g\ kg^{-1}$, or 5 ppb, is needed. To know whether intake is significantly below 10 $\mu g\ day^{-1}$, a quantitation limit of about 1 $\mu g\ kg^{-1}$ is needed. Work is ongoing in FDA's laboratories to develop the reliable, quantitative methods that will be required to track the continuously dropping levels of lead in the US diet (Capar, 1991).

One difficulty with using the TDS to make generalized exposure estimates is that it models the diets of average individuals in the US. it is difficult to use the TDS to generate exposure estimates for non-average eaters such as high percentile consumers or eaters of ethnic foods. To address this problem, a computer database that will be a combination of the TDS data on lead and the food intake information found in the recently released 1987–88 USDA National Food Consumption Survey is being created. The end result will allow production of updates to our lead exposure estimates as new analytical data on lead levels in foods are received. In addition, it will allow calculation of lead exposure from hypothetical diets and estimation of lead consumption by susceptible groups or individuals.

The USDA survey is a three-day record of consumption. Over 38,000 individuals participated, and these participants were divided into 16 age-sex groups. Our initial interest is in creating a system that will allow us to estimate dietary lead intake from specific foods by age and sex of the consumer. In addition, we want to be able to break down our exposure estimates by consumption percentile.

As previously mentioned, the USDA National Food Consumption Survey catalogues over 5,000 foods including ethnic foods and many foods prepared from multiple ingredients. Each of the 234 foods in the TDS represents one or more of the over 5,000 foods in the USDA database. By assigning the lead content of a representative TDS food item to the USDA foods it represents, approximate lead values can be quickly assigned to the entire USDA database. For USDA foods that are combinations of ingredients, such as the listing for the food described as 'beef stew with potatoes', the USDA has recipes specifying the proportions of ingredients. By assigning separate lead values to beef and to potatoes, a weighted average lead content for the dish can be determined. The computer program that is envisioned will generate an intake report for lead, or for any other contaminant for which we have analytical data, for any diet that is specified. Another advantage of the computerized system is that when new analytical data are obtained, the lead values of all the foods can be quickly and automatically adjusted. Thus, we hope to have a system soon that will allow us to develop lead intake data for specific age–sex groups, for ethnic diets and for high-level consumers.

In summary, the TDS helps to fulfill the FDA's responsibilities of determining the incidence and level of selected contaminants, pesticide residues and nutrients in the food supply, and it helps to promote consumer confidence. It provides 'real world' dietary exposure information about food as it is actually consumed. This information has been consistently used by Congress, consumer groups and other interested organizations. The TDS has proved to be invaluable to the FDA in monitoring trends in the food supply, and there is no doubt that it will continue to provide a measure of the effectiveness of US regulations and initiatives on lead reduction.

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A Guide to Interpreting Soil Ingestion Studies. 1. Development of a Model to Estimate the Soil Ingestion Detection Level of Soil Ingestion Studies

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Abstract

This paper provides a model to predict soil ingestion recovery values in soil ingestion studies either retrospectively or prospectively. The predictive equations generated from the model can be used to estimate minimum soil ingestion detection levels from soil ingestion studies which use mass–balance methods. The model is derived from data assessing soil recovery efficiencies in adults using eight different predictive tracer elements. The results constitute a methodology to determine minimum detection levels of soil ingestion, and hence have important regulatory significance.

Introduction

Soil ingestion by children has become an important issue in assessing public health risks at sites with tightly bound contaminates such as lead, PCBs, and dioxin. Several studies have been completed which have attempted to estimate the amount of soil ingested by children (Binder *et al.*, 1986; Clausing *et al.*, 1987; Calabrese *et al.*, 1989; Davis *et al.*, 1990; van Wijnen *et al.*, 1990), and one for adults (Calabrese *et al.*, 1990). While each of these studies derived estimates of soil ingestion for their subjects, none of these studies published the level of detection of soil ingestion for their respective study groups.

In this paper, we develop a methodology for assessing the precision of soil ingestion estimates for a particular tracer element, based on percent tracer recovery data from an experimental study among six adults. Although the results are based on a small number of subjects, the methods developed are sufficiently general that they may be applied to studies of soil ingestion retrospectively or prospectively. Since wide differences in soil ingestion estimates have been observed in individual studies of children, the methodology provides a strategy for identification of reliable soil ingestion estimates (and quantifying the precision of the estimate). Thus, this paper will present a methodology to determine the soil ingestion detection limit of a soil ingestion study. The models developed will be applied to other current published studies in Part 2.

The Soil Tracer Methodology

Soil tracer methodology is based on the assumption that elements in soil that are employed in the methodology are not absorbed or involved in the metabolic pathway. The basic concept behind the soil tracer method is that when a subject is in equilibrium, the intake of an element from inhalation and ingestion (food and water) will equal the output of the element in feces and urine. This equivalence can be expressed as a mass balance equation for a particular tracer element:

$$I_a + I_{fo} + I_s + I_w = O_f + O_u$$

where

I_a = amount of tracer element from air
= $A_c \times A_a$
= (air concentration) × (amount of air inhaled)

I_{fo} = amount of tracer element from eating food
= $F_{fo} \times F_a$
= (food concentration) × (amount of food ingested)

I_s = amount of tracer element from soil
= $S_c \times S_a$
= (soil concentration) × (amount of soil ingested)

I_w = amount of tracer element from water
= $W_c \times W_a$
= (water concentration) × (amount of water ingested)

O_f = amount of tracer element from feces
= $F_c \times F_a$
= (fecal concentration) × (amount of feces)

O_u = amount of tracer element from urine
= $U_c \times U_a$
= (urine concentration) × (amount of urine).

Knowledge of each aspect of the equation, with the exception of amount of soil (S_a), will permit estimation of the amount of soil ingested.

In practice, not all parts of the mass balance equation are of equal importance. Soil ingestion studies based on a tracer methodology have not emphasized sources of intake due to air and water, and sources of output due to urine due to their generally negligible impact on the outcome. The simplified mass balance equation is as follows:

$$I_{fo} + I_s = O_f$$

† *Special issue incorporating the Proceedings of the Symposium on the Bioavailability and Dietary Exposure of Lead.*

which results in the soil ingestion esumate:

$$S_s = (O_f - I_{fo})/S_c$$

$$\text{(amount soil ingested)} = \frac{\text{(element fecal} - \text{element ingested)}}{\text{(conc soil)}}$$

It is this equation that has been the source of soil ingestion estimates using the tracer methodology for all of the above cited studies.

Evaluating the Precision of Soil Ingestion Estimates for Tracers

The ideal tracer element for soil ingestion estimation studies is one that is not present in food (or water or air or medications), is uniformly present in high concentrations in soil, and is poorly absorbed via the gastrointestinal tract. No element meets these criteria, since all tracers have been found in food, and most are present in relatively low concentrations in soil. However, the soil ingestion equation permits estimation of soil ingestion even when a tracer is present in the food, since this amount can be simply subtracted from the amount of tracer output within the context of a mass–balance study. This subtraction assumes a one to one correspondence between tracer intake from food and other products (*e.g.* medications) and the amount of the tracer from food in the fecal output.

The accounting for food in the soil ingestion equation is valid if there is a one-to-one correspondence between tracer food input and tracer output. This correspondence does not hold for two interrelated reasons. First, the amount of a tracer ingested from food varies for a subject from day to day. Second, the transit time for food from ingestion to feces varies from day to day. As a result of these two sources of variability, the quantity of a tracer in feces in a given day will represent the quantity ingested in solid food, liquids, medications, *etc.* (plus the quantity ingested from soil) over some previous time period. If a subject were followed for a long period of time with continuous measurement of a tracer in food intake and fecal output, one could argue that the amount of the tracer from food should balance the amount of the tracer in the fecal output from food. In practice, the correspondence may be poor. Practical considerations have limited the time that a subject is followed with continuous food intake and fecal output measures to 3–4 days. Large discrepancies between tracer intake from food and tracer amount due to food in fecal output are possible over short observation periods.

The basic lack of temporal correspondence between intake and output can be resolved by designing longer, more expensive studies. However, in the context of currently conducted studies some evaluation can be made of the potential for a tracer to be subject to 'time' errors. Tracers with low levels in food will not be influenced greatly by differing food intake or varying transit times. Additionally, the variability in food intake will have a relatively smaller effect on tracers that have high concentrations in soil. If a known quantity of soil were ingested, then a simple measure of the impact of food on that tracer is the ratio of the amount of a tracer in food to the amount of a tracer in the ingested soil, *i.e.* $R = I_{fo}/I_s$. Low ratios indicate a reliable tracer. Higher ratios indicate progressively less reliable tracers. Examples of these ratios from Calabrese *et al.* (1990) based on median food intake for six adults (total of 17 subject/weeks) assuming a consumption of 100 mg of Northhampton soil day^{-1} are given in Table 1.

Table 1 *Ratio of food/(100 mg Northampton soil) for six adults.*

Al	0.145	Ti	2.50
Ba	10.3	V	0.422
Mn	28.8	Y	0.441
Si	1.04	Zr	0.0893

Results based on Calabrese *et al.*

The ratios in Table 1 provide a qualitative assessment the relative precision soil ingestion estimates based on th elements. A quantitative assessment of precision for s ingestion estimation requires actual data on percent recover soil. Such data are available from an experimental study on adults who were administered a specified quantity of s (Calabrese *et al.*, 1990). Using such data and the mass bala equation, a model can be developed for the precision of perc recovery of soil. We develop a model for the average absol deviation in the percent recovery of soil about 100% (the m square error in percent recovery) using the food/soil ratio a predictor variable. We first briefly review the adult stu design. The remainder of the paper presents the model development and results evaluating the model.

An Adult Experimental Study of Soil Ingestion

An experimental study of the tracer methodology w conducted by Calabrese *et al.* (1990) in Amherst, MA. Six participants consisted of six healthy adults, three males a three females, 25–41 years old. The study was conducted ov three weeks. Each participant ingested one capsule at breakfa and one capsule at dinner on Monday, Tuesday, and Wednesd of each week. During the first week, the capsules ingested we empty; during the second week, each capsule contained 50 m of sterilized soil; during the third week, each capsule contain 250 mg of sterilized soil. Duplicate meal samples, food an beverage were collected from breakfast on Monday through th evening meal on Wednesday for each subject in each week. A medications were included in the samples. Total excretor output, feces and urine, were collected from Monday noo through Friday noon of each week. Laboratory analyse estimated on a daily basis the total amount of eight tracers (A Ba, Mn, Si, Ti, V, Y, and Zr) ingested from food, from capsu doses, and in the fecal and urine output. The results were use to form a single estimate for each week and element of dail intake from food, intake from soil, and total fecal and urin output. More details of the methods and results are given b Calabrese *et al.* (1990).

Model Development

Since soil ingestion was controlled in the adult study, it i possible to model the variability in soil ingestion estimates du to variable food intake and transit time. As a first step in mode development, the ratio of the average daily amount per week o a tracer ingested from food to the average daily amount ingeste per week from the capsules (*i.e.* R) was calculated for eac

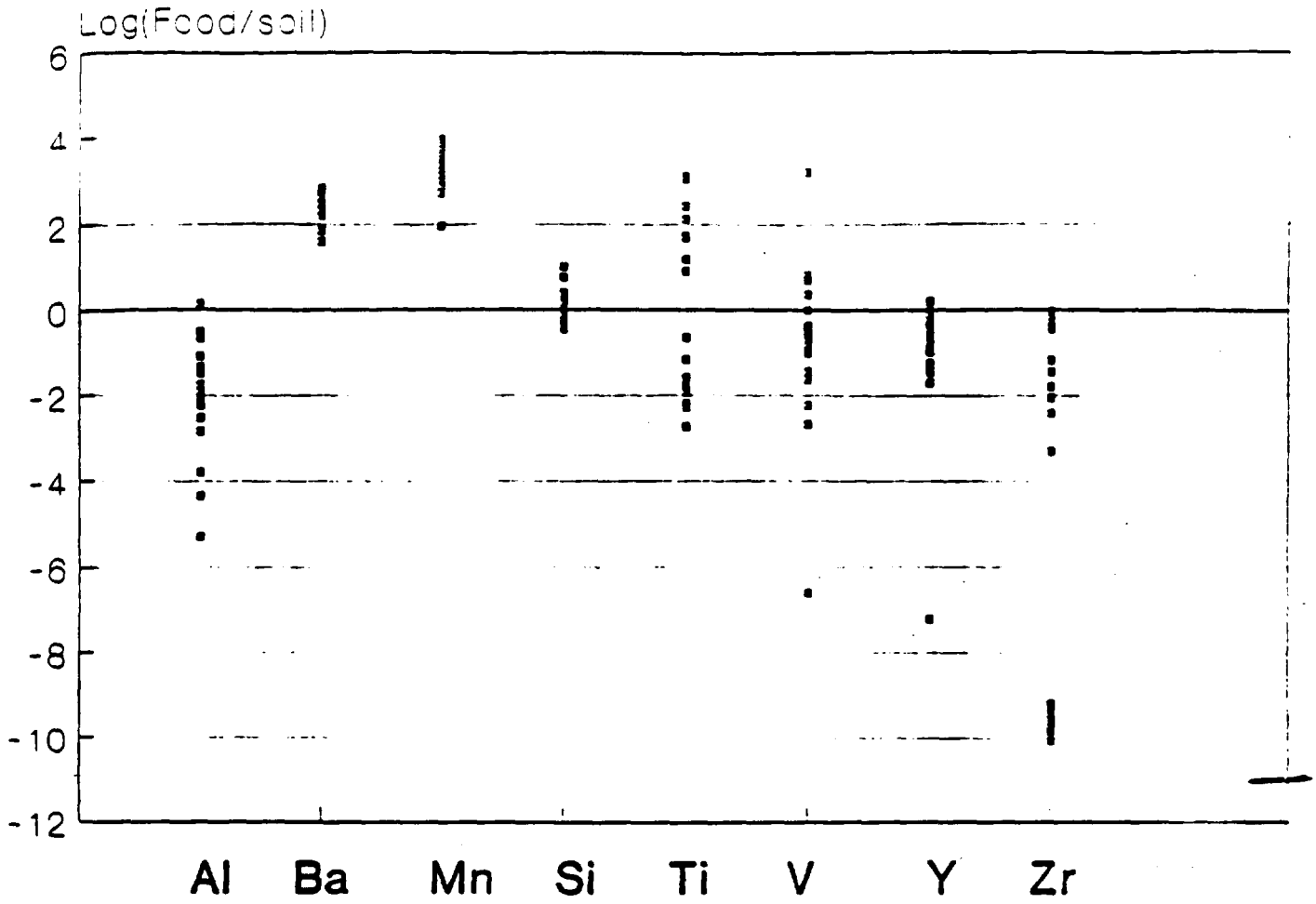


Figure 1 *Distribution of log(food/soil) ratio for six adults by element and week.*

week for week two and three for each subject. When the concentration of an element in food was less than the detection limit for a given day, the detection limit concentration (see Stanek *et al.*, 1988; Table II, p.183) was multiplied by the amount of food ingested to estimate element ingestion. Of the 36 daily food ingestion estimates recorded, concentrations were less than the detection limit on one or more days for five elements (17% of days for Al; 6% of days for Ti; 17% of days for V; 28% of days for Y; and 64% of days for Zr). For two elements (Y, and Zr), no detectable amount of the element was reported in food on any day in 1 and 5 subject-weeks, respectively. The weekly food/soil ratios by element are summarized in Figure 1. The natural logarithm was used for presentation since the range of food/soil ratios was large.

The distribution of weekly log (food/soil) ratios in Figure 1 indicated a broad range of ratios for all elements. For Y, and Zr, weeks with no detectable element ingestion from food had log (food/soil) ratios that were substantially different from the observed detectable distribution. These subject-week values (*i.e.* when no detectable food tracer value occurred during that week) were excluded from subsequent calculations so as to avoid undue influence on the results. Percent soil recovery was estimated for each subject-week and element by calculating the average daily fecal output (O_f), the average daily food intake (I_{fo}), and the average daily capsule dose (I_{se}) for each subject. Averages for fecal output and capsule dose were calculated over four days, while averages for food intake were calculated over three days. Percent recovery was then calculated as:

$$\text{Percent recovery} = 100 \times (O_f - I_{fo})/I_{se}.$$

Figure 2 illustrates a plot of percent recovery against the log (food/soil) ratios for the second and third weeks. Since no soil was ingested by capsule in the first week, no percent recovery could be calculated for that week. Each point in the plot is specific for a subject-week and element. The figure indicates the anticipated pattern of larger variability in log (percent recovery) with higher food/soil ratios.

Variability in percent recovery was quantified by forming six food/soil ratios groups with equal numbers of observations in each group. For each group, the mean square error in percent recovery was calculated as the average squared deviation in the percent recovery from 100%. The mean square error was used as the measure of variability for soil ingestion. The results for the six groups are summarized in Table 2.

A plot of the log (MSE % recovery) versus the log of the median food/soil ratios in Figure 3 illustrates a linear relationship between variability in percent recovery and food/soil ratios. Superimposed on the plot is the estimated linear regression equation from a model to predict log (MSE % recovery) from the median log (food/soil) ratios. The resulting

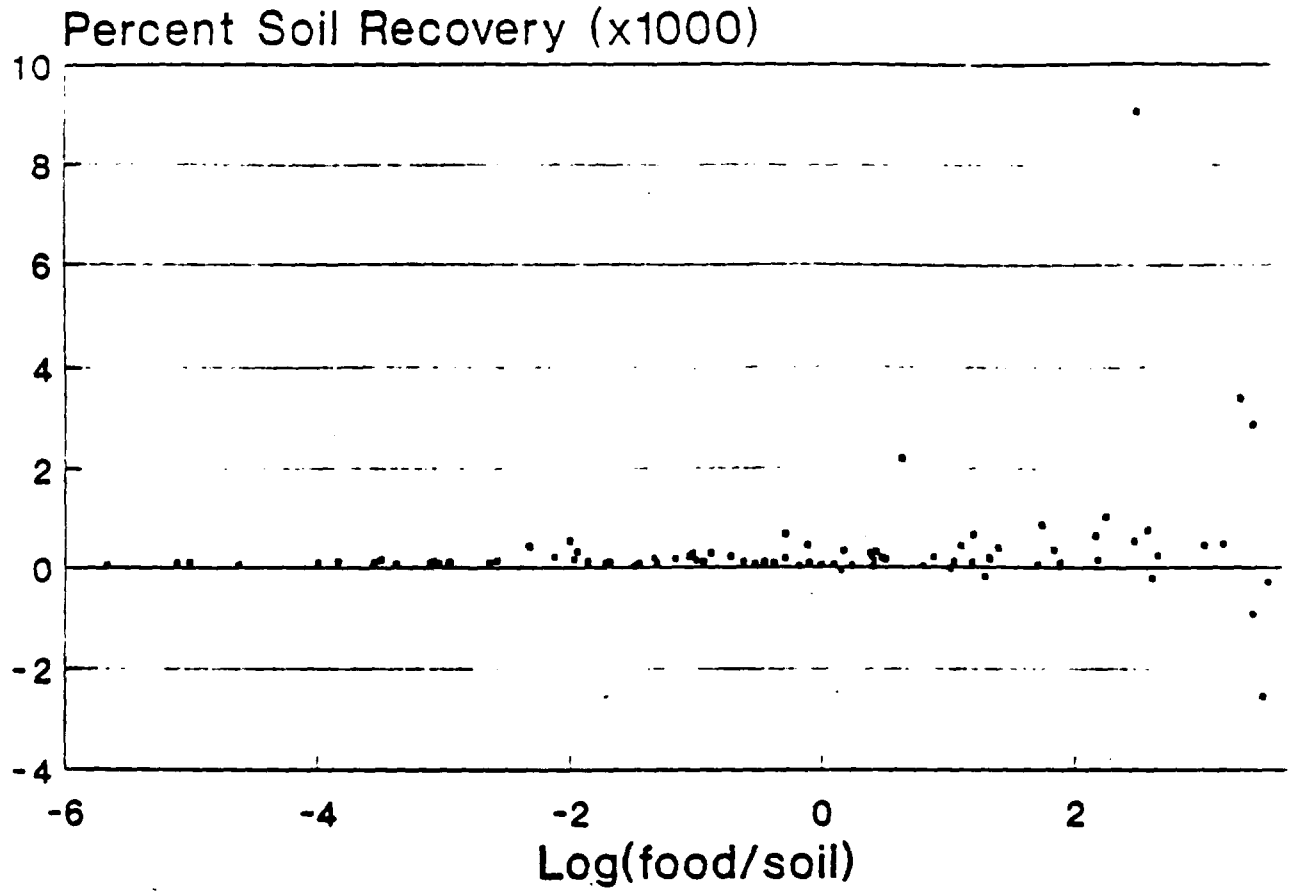


Figure 2 *Plot of percent recovery versus log(food/soil) for six subjects, 2 weeks.*

model predicted 89.5% of the variability in log (MSE % recovery), with a residual square error of 1.21. The regression equation was:

$$\log(\text{MSE percent recovery}) = 11.4 + 1.227 \log(R) \quad (1)$$
$$(0.45)\ (0.21)$$

with standard errors of regression coefficients reported in parentheses.

Table 2 *Results of six group formation for food/soil ratios and log (mean square error) in percent recovery.*

Group	Range in food/soil (R)	Median food/soil recovery)	log (MSE for percent
1	0.000–0.075	0.0285	6.62
2	0.075–0.300	0.156	10.1
3	0.300–0.900	0.533	10.5
4	0.900–2.300	1.47	12.6
5	2.300–8.700	3.73	11.5
6	8.700+	20.66	15.8

Model Implications

The regression model has implications for estimatin precision of individual soil ingestion estimates, an extension, implications for estimating soil ingestion population. Variability (as estimated by the standard devia *i.e.* the square root of the MSE) should be small for estim to be precise. We use one standard deviation as a measu this precision. Table 3 presents examples of standard devia (expressed as percent) and the accompanying maxi food/soil ratios based on Equation 1. If the food/soil exceeds the maximum in Table 3, then one standard dev in the percent soil recovery will exceed the specified lev the row in the table. Table 3 also summarizes the obs proportion of subject/weeks in the adult study that foo ratios were lower than the calculated maximum amount (*i.* proportion of subject-weeks that meet or exceed the spec level of precision).

The results indicate that large amounts of soil, and/or small amounts of food are required to have low stan deviations in the percent recovery. In the study of 6 adults element that proved to be most reliable was Al. Even for element, however, one standard deviation was less than or e to 50% for only 18% of the subject-weeks.

The results presented in Table 3 imply that variabili

Table 3 *Predicted standard deviation (SD) of percent recovery of soil for a subject and food/soil ratios based on hypothetical 100 mg ingestion of Northhampton soil from equation (1).*

Percent recovery (± 1 SD)	Maximum food/soil ratio (R) to yield SD in % rec.	Percent likelihood that a subject would have a food/soil ratio less than or equal to the indicated value by element*							
		Al	Ba	Mn	Si	Ti	V	Y	Zr
100 ± 5	0.00126	0	0	0	0	0	0	0	0
100 ± 10	0.00391	0	0	0	0	0	0	0	0
100 ± 20	0.0121	6	0	0	0	0	0	0	0
100 ± 50	0.0539	18	0	0	0	0	0	0	10
100 ± 100	0.167	53	0	0	0	29	12	0	40
100 ± 200	0.516	82	0	0	0	47	56	63	60
100 ± 500	2.30	100	0	0	94	47	94	100	100

* Based on 17 subject-weeks for Al, Ba, Mn, Si, Ti; 16 subject-weeks for V, Y; and 10 subject-weeks for Zr.

percent recovery of soil is sufficiently great using the Calabrese *et al.* study design so as to prevent accurate prediction of individual soil ingestion, unless soil ingestion is at high levels. Although individual soil ingestion may not be predicted with confidence, the population median (or average) soil ingestion can be predicted with more confidence. This is based on standard statistical theory, indicating that the standard error of the estimated population mean percent recovery is inversely proportional to the square root of the sample size (Daniel, 1987). The larger the sample size, the higher the confidence in the estimate of the percent recovery.

Equation 1 can be used to predict the maximum food/soil ratio that will result in a given standard error in percent recovery for a study population, accounting for sample size. This equation is given as:

$$R = \exp(\{\ln(n) + \ln(MSE) - 11.4\}/1.227) \quad (2)$$

where n = number of subjects in the study population,

MSE = MSE of percent soil recovery for a single subject,

R = maximum food/soil ratio necessary to have the mean square error of the percent recovery for the study population average be equal to MSE/n.

Using this equation, the degree of precision in percent recovery is summarized for various size study populations in Table 4.

Table 4 can be used to estimate the degree of precision in the mean estimate of soil ingestion for a population based on the sample size and food/soil ratios observed in a given study. The results summarize the impact of number of subjects on the standard error in percent soil recovery assuming there is one measure per subject. When studies record more than one measure per subject (as in Calabrese *et al.* 1989, and Calabrese *et al.* 1990), further information is needed to know whether to use as n the number of subjects, or the number of subject-weeks in estimating the standard error in percent recovery. If there is a large subject component in the variability in percent recovery, the number of subjects should be used as n. If the subject component in the variability in percent recovery is minimal, the number of subject-weeks should be used as n.

Since the Calabrese *et al.* (1990) study evaluated adults for more than one week per subject, it was possible to evaluate

Table 4 *Maximum food/soil ratios (R) required to yield a specified standard error in the percent recovery, based on equation (2).*

Number of subjects (n)	Maximum food/soil ratios (R) required (percent recovery ± 1 SE)			
	100 ± 5	100 ± 10	100 ± 20	100 ± 50
1	0.0013	0.0039	0.0122	0.0542
10	0.0083	0.0257	0.0796	0.354
30	0.0203	0.0629	0.195	0.867
60	0.0358	0.111	0.343	1.53
100	0.0542	0.168	0.520	2.31
400	0.1679	0.520	1.61	7.16

whether n should represent the number of subjects, or the number of subject weeks. To answer this question, analysis of variance models were fit to deviations from 100% recovery for the six adults. Components of variance in percent recovery due to subject, and due to subject-week were evaluated. Four models were fit using different dependent variables. The dependent variable for the first model was the simple deviation in recovery, calculated as the difference between the soil ingestion estimate and the capsule ingestion for each of the subjects for each of three weeks for each of eight elements. The dependent variable for the second model was similar to the first, where the deviation in recovery was calculated as the predicted deviation based on equation (1). Two additional models were fit using the log of these deviations as the dependent variable.

The proportion of variation due to subjects was estimated as zero for models using the actual deviation, and 20% and 11%, respectively for models with dependent variables corresponding to the log deviations and log predicted deviations. In both models based on the logarithm, the component of variance due to subject was not statistically significant. These results indicate that the subject component of variance is small (or zero) relative to the week to week component of variance. These results imply that the number of subject-weeks should be used as the sample

Table 5 *Estimates of daily ingestion (I_{fo}) of trace elements in food.*

Element	6 adults[a] 17 weeks Median	Mean	64 children[b] 128 weeks Median	Mean	101 children[c] 101 weeks Median
Al (mg)	1.2	2.4	1.2	1.9	5.6
Ba (mg)	0.61	0.64	0.22	0.27	
Mn (mg)	2.4	2.5	1.3	1.5	
Si (mg)	29.0	32.0	14.0	17.0	20.0
Ti (mg)	1.3	2.6	0.20	1.0	0.64
V (μg)	5.9	29.0	5.3	9.0	
Y (μg)	1.1	1.3	1.1	1.9	
Zr (μg)	1.6	4.3	2.5	6.7	

[a] Calabrese *et al.*, 1990.
[b] Calabrese *et al.*, 1989.
[c] Davis *et al.*, 1990.

Table 6 *Estimates of trace element concentration (S_c) in soil.*

Element	Northhampton[a] MA Median	Mean	Amherst[b] MA Median	Mean	East Helena[c] MO Median	Mean	Southeastern[d] Washington State Median	Mean	Wageningen[e] Holland Median	Mean
Al (mg g^{-1})	81	55	53	67	67	66	66	17.8	18.3	
Ba (mg g^{-1})	0.59	0.33	0.34							
Mn (mg g^{-1})		0.82	0.73	0.71						
Si (mg g^{-1})	280	320	300	300	300	290	290			
Ti (mg g^{-1})	5.2	3.4	3.3	2.9	3.0	5.8	5.8	0.72	0.79	
V (μg g^{-1})	140	65	69							
Y (μg g^{-1})	24	24	24							
Zr (μg g^{-1})	180	190	180							

[a] Calabrese *et al.*, 1990.
[b] Calabrese *et al.*, 1989.
[c] Binder *et al.*, 1986.
[d] Davis *et al.* (1990)
[e] Clausing *et al.*, 1987.

size when multiple measures are made on subjects for evaluation of studies similar to the adult study design of Calabrese *et al.* (1990).

In order to evaluate the precision of population soil ingestion estimates in particular studies, equation 2 can be re-expressed by expanding the determinants of R, the food/soil element ratio, and solving for the amount of soil ingested. The resulting equation is:

$$S_s = I_e \exp\{[11.4 - \ln(n) - \ln(\mathrm{MSE})]/1.227\}/S_c \qquad (3)$$

where S_s = the amount of soil ingested day^{-1}
I_e = the amount of a particular element ingested day^{-1} from food
n = the number of subjects (or subject-weeks) in the study
MSE = the mean square error in percent recovery of soil for a subject. (*i.e.* SD % recovery = 20% implies that MSE = 400)
S_c = the concentration of the particular element in soil

Equation (3) provides an expression for the 'det limit' for soil ingestion with a specified level of pre (MSE) from a particular study. The equation depends c amount of the element ingested in food, and the correspo concentration of the tracer element in soil. Exampl published estimates of the daily amount of elements inges food are given in Table 5. Estimates of concentratio elements in soil from published studies are given in Tabl

The estimates of element ingestion from food and el concentration in soil from Tables 5 and 6 can be us equation (3) to generate plots of detectable levels of soil sample size for a given level of precision. Figures 4 contain such plots for the Calabrese *et al.* (1990) adult based on Northhampton soil concentrations, and medi mean adult food ingestion, assuming a 20% standard er percent recovery.

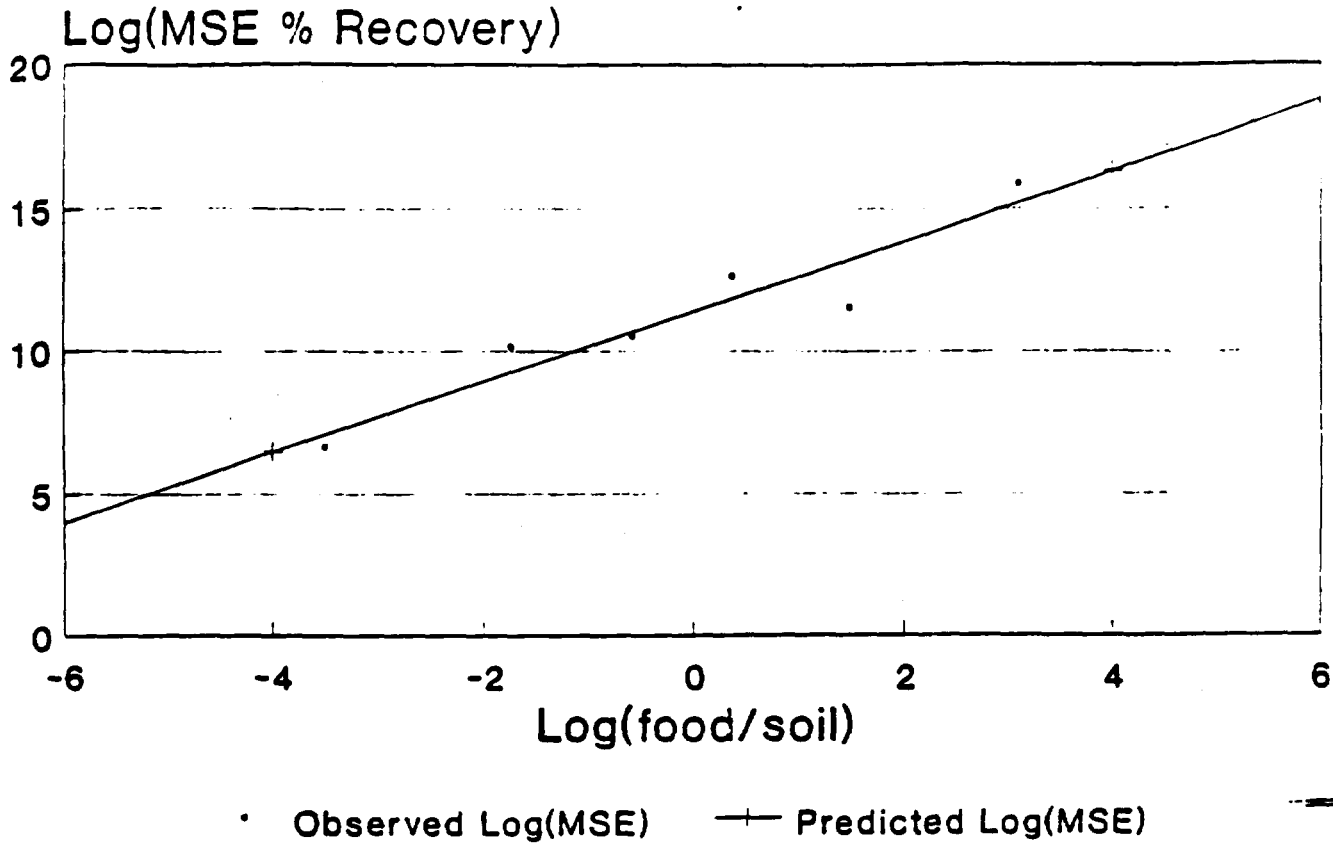
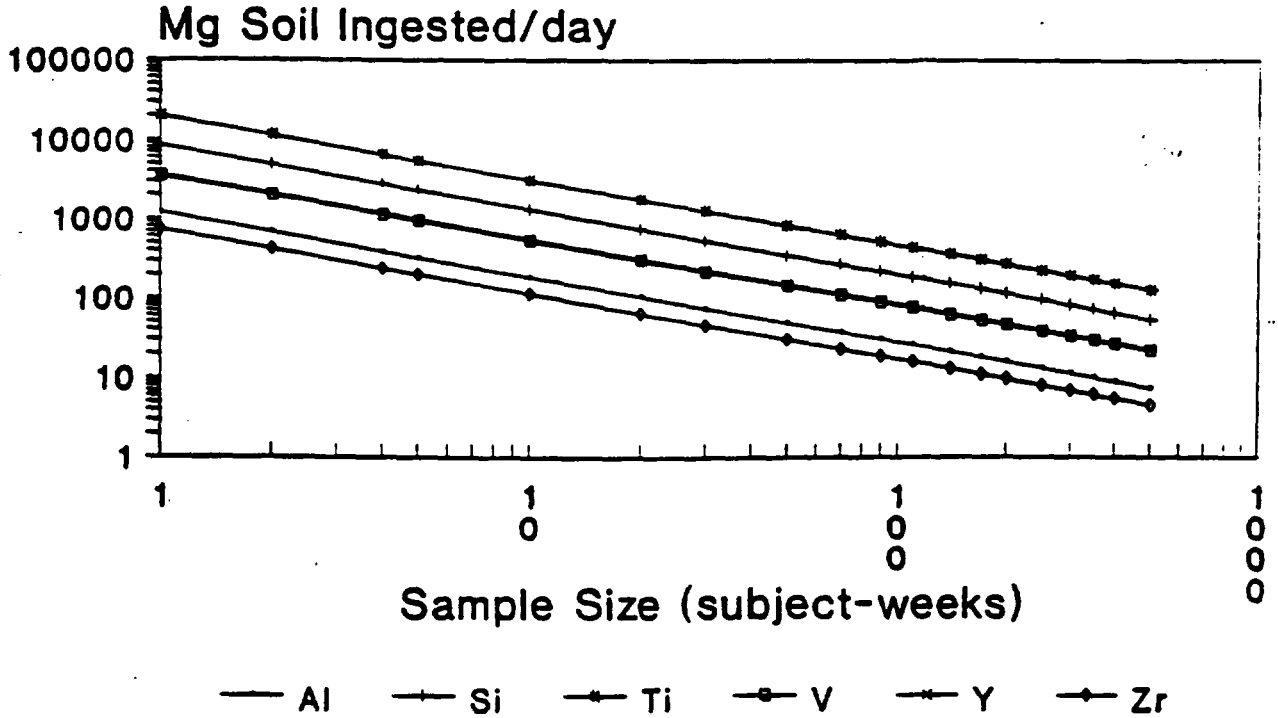


Figure 3 *Plot of log(MSE percent recovery) versus log(food/soil) for six food/soil groups*



Using Northhampton Soil Concentrations

Figure 4 *Sample size versus soil ingestion (mg) assuming 12E in percent recovery = 20% based on median adult food ingestion.*

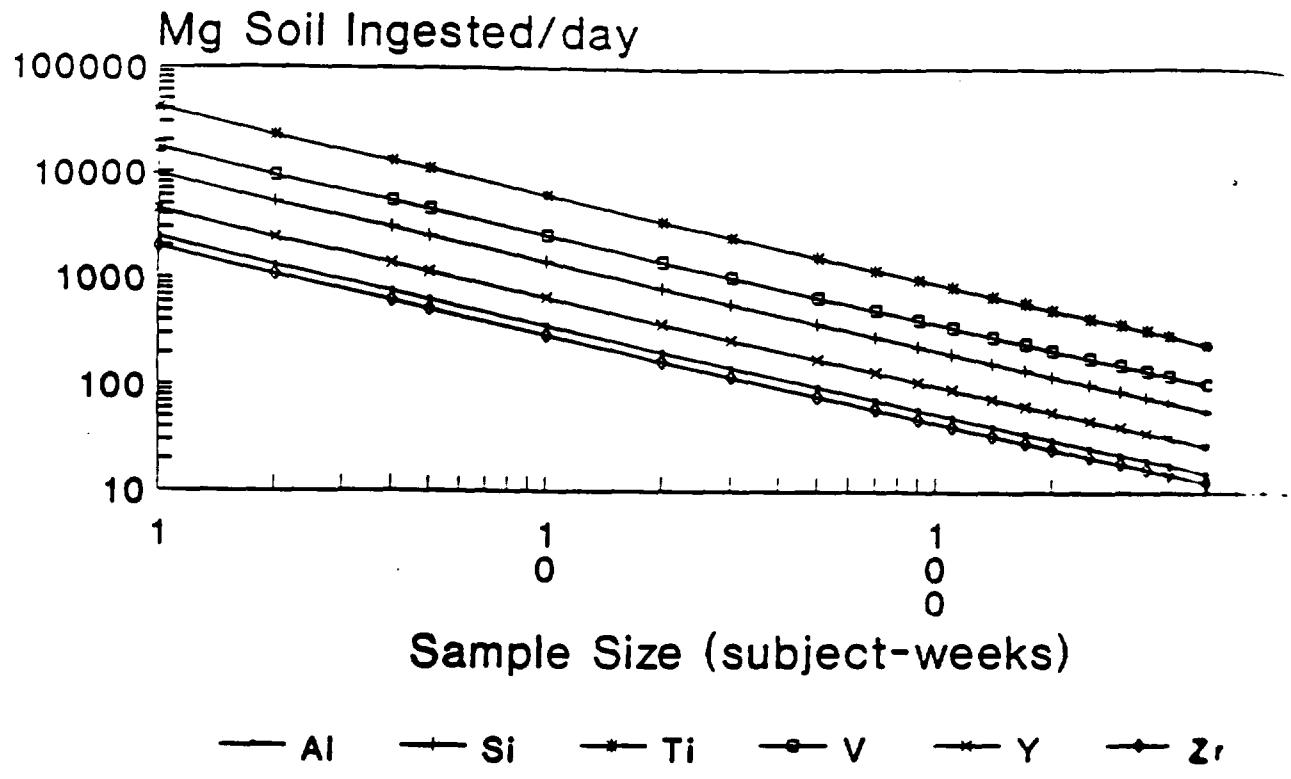


Figure 5 *Sample size versus soil ingestion (mg) assuming 12E in percent recovery = 20% based on median adult*

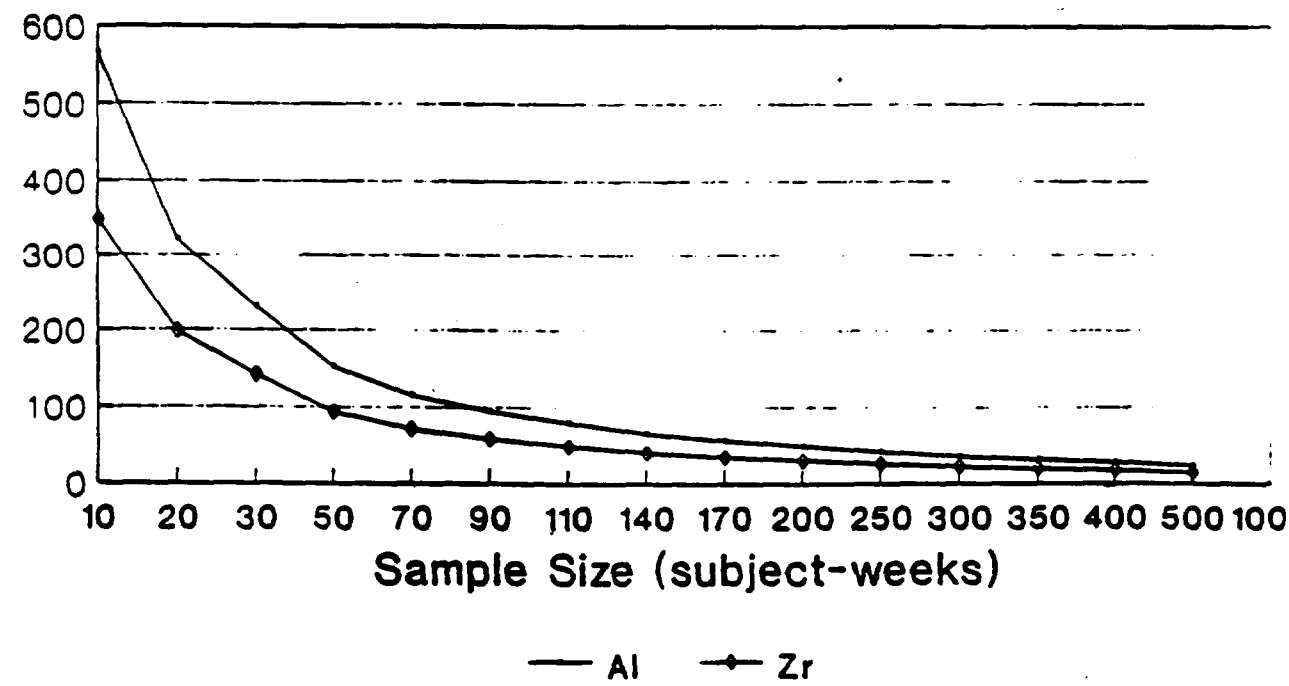


Figure 6 *Sample size versus soil ingestion (mg) assuming 2SE in percent recovery = 20% based on median adult food ingestio*

Table 7 *Approximate 95% confidence interval estimates for soil ingestion in children based on predicted percent recovery variance and food/soil element concentrations.*

Study[a]	Element	n	Median	95% CI	Mean	95% CI
Calabrese	Al	128	29	(16,42)	153	(121,185)
Calabrese	Ba	128	<0	NA	32	(0,8492)
Calabrese	Si	128	40	(17,63)	154	(112,196)
Calabrese	Ti	128	55	(25,85)	218	(80,357)
Calabrese	V	128	96	(50,142)	459	(342,576)
Calabrese	Y	128	9	(0,22)	85	(41,129)
Calabrese	Zr	128	16	(8,24)	21	(6,36)
Calabrese	Al	64	29	(11,47)	153	(108,198)
Calabrese	Ba	64	<0	NA	32	(0,11996)
Calabrese	Si	64	40	(8,72)	154	(95,213)
Calabrese	Ti	64	55	(12,98)	218	(22,414)
Calabrese	V	64	96	(31,161)	459	(294,624)
Calabrese	Y	64	9	(0,27)	85	(23,147)
Calabrese	Zr	64	16	(5,27)	21	(0,43)
Davis	Al	101	25	(0,57)	39	(0,82)
Davis	Si	101	59	(21,97)	82	(34,131)
Davis	Ti	101	81	(22,139)	246	(63,428)

[a] Calabrese *et al.*, 1989 and Davis *et al.*, 1990.
NA – not applicable due to negative estimates

If the detection limit for a study is defined as 2 SE in the % recovery = 20%, then similar figures can be used to estimate the detection limit for the median or mean soil ingestion estimate in the study population. Figure 6 contains a similar plot on a different scale illustrating the detection limits based on the median adult food ingestion with 2 SE in the % recovery = 20%. Since the Calabrese *et al.* (1990) study included 17 subject-weeks of observation, the minimum amount of soil that could be detected with 20% (= 2 standard errors) in percent recovery is estimated as 374 mg for Al, and 224 mg for Zr. Similar detection limits can be calculated for other studies.

The choice of mean or median food ingestion makes a substantial difference when evaluating the amount of soil that can be detected for a given standard error in percent recovery. The estimate of detectable soil ingestion from equation (3) assumes that all subjects in the study have the same food intake. If that common food intake is the median intake, then the estimate of the detectable median amount of soil results. Since food ingestion is not normally distributed (but skewed to the right), the average food ingestion is higher from the median intake. Although the average intake may not correspond to the actual intake of any particular subject, the evaluation of soil detection assuming all subjects ingest the average intake results in a detection limit more appropriate for an average soil ingestion estimate.

Equation (2) can also used to estimate confidence intervals for population median or mean soil ingestion estimates based on particular elements. Approximate 95% confidence interval estimates are given by the expression:

$$S_e \pm 2\, S_e \exp(0.5[11.4 + 1.227 \ln (I_e/(S_c\, S_e)) - \ln (n)]) \quad (4)$$

Using values of S_e from Calabrese *et al.* (1990 [illegible] *et al.* (1990), I_e from Table 5, and S_c from Table [illegible] median concentrations), and reported sample (or [illegible]) sample sizes, approximate 95% confidence interval [illegible] can be made for the population soil ingestion. These [illegible] are given in Table 7. For comparison, confidence interval estimates are included for Calabrese *et al.* (1989) based on n = 128 subject-weeks and n = 64 subjects.

Discussion

The methodology presented in this paper offers a way of quantifying precision of soil ingestion, and the detection limit for soil estimation from existing studies. The results are of importance in evaluating existing studies, and are relevant to future soil ingestion studies. For existing studies, the methods provide a rationale for selecting elements for quantifying soil ingestion that are most reliable. For design of new studies, the results allow elements to be screened based on the food/soil ratios prior to study conduct, and permit sample size calculations to be made that reflect a specified level of precision.

Although the methods and results may be useful in quantifying soil ingestion, there are three aspects of the current study that are important in interpreting the results. First, the study results are limited by the small number of subjects (n = 6, 12 subject-weeks per tracer) used to calculate all equations. A larger, more diverse study population would clearly be desirable. Within this context, it is important to note that only seven subject-weeks were included for Zr due to Zr food ingestion values less than the detection limit in five weeks.

Table 8 *Effect of alternative assumptions on casual soil ingestion in adults on approximate 95% confidence interval estimates for median soil ingestion (mg day^{-1}) in children based on predicted percent recovery variance and food/soil Al concentration.*

Assumed adult daily soil ingestion (mg day^{-1})	Calabrese $n = 128$		Calabrese $n = 64$		Davis $n = 101$	
	Lower	Upper	Lower	Upper	Lower	Upper
0	16	42	11	47	0	57
10	16	42	10	48	0	59
25	15	43	9	49	0	61
50	15	44	8	50	0	65
100	10	48	2	56	0	75

We feel that the decision to exclude weeks with less than detectable food intake for particular elements from the analysis will serve to make the results more robust. Since all analyses are based on a log scale, and log (0) approaches minus infinity, using the logarithm of the detection limit or some fraction of the detection limit may have a large influence on the modelling results. This influence will depend on the somewhat arbitrary choice of values used to replace the detection limit. This problem was avoided by excluding subject-weeks with less than detectable food intake for an element.

In contrast, when one or more detectable values of a particular element were recorded in a given week, we used the detection limit for days in that week when the element was less than detectable prior to calculating an average food ingestion estimate for that week. This decision had minimal impact on the results, since detectable ingestion of food nearly always exceeded the detection limit by one or more orders of magnitude. As a result, averaging in the detection limit, or using zero as the estimate of food ingestion when ingestion was less than detectable had little influence on the resulting food ingestion average for the week.

A second aspect of the study that is important in interpreting results is the dependence of results on the adult study protocol. All models were developed based on 3-day average estimates of element intake from food, and 4-day average estimates of element output in the feces. Although the average daily food intake and output may not be affected by varying study collection protocols, longer food–fecal collection protocols should increase correspondence between food and feces. This increased correspondence should increase the precision of soil estimates. As a result, the prediction equations may not be valid for studies with food–fecal collection protocols that differ from the Calabrese *et al.* (1990) study. For studies with shorter collection protocols, the results may be considered a lower bound for prediction of soil ingestion detection limits. For studies with longer collection periods, the soil ingestion estimates may be more reliable. In addition, since the equations are derived from adult data, the appropriateness of applying study results to children, although plausible, can not be confirmed.

A final aspect of the present study that is important in interpreting study results is the assumption throughout the model development that study subjects did not ingest soil other than from capsules administered in the study. Calabrese (1990) provides casual soil ingestion estimates for adult suggest that a zero soil estimate is unreasonable. To ev the impact of casual soil ingestion estimates on equation re-evaluated the regression equation assuming 10, 25, 50, mg day^{-1} soil ingestion per adult. The resulting para estimates were then used in equation (4) to calc approximate 95% confidence intervals for median soil ing similar to Table 7. The effect of different assumptions similar for each element, so we present only results based in Table 8.

Although the regression coefficients change different assumptions of casual soil ingestion among a confidence intervals are affected only modestly hypothesized adult ingestion levels of less than 50 mg With larger hypothesized soil ingestion for adults, the wi the confidence intervals increased.

The models presented in this report predict variabili soil ingestion solely on the food/soil ratios. Another facto may be important in evaluating potential tracers for ingestion estimation is variability in daily food intake. Ele with more highly variable food intake are more likely to correspondence between food intake and fecal output per for studies with protocols comparable to those cited. Additi models were developed to assess the effect of daily variab in food intake in conjunction with the food/soil rati estimating the log (MSE % recovery). These models indic that daily variability in food intake was positively assoc with log (MSE % recovery), but less important that the food ratio. However, sample sizes were too small using these da have confidence in projecting detection limits based on the variable model. Still, this factor should be considered in de of future studies to quantify soil ingestion.

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A Guide to Interpreting Soil Ingestion Studies. 2. Qualitative and Quantitative Evidence of Soil Ingestion

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Abstract

Four major studies have attempted to qualitatively and quantitatively assess the extent of soil ingestion in children using the soil tracer methodology. The validity of the estimates of soil ingestion of each study was reevaluated in light of the inherent strengths and limitations of study design and/or execution as well as via a novel methodology to estimate the soil recovery variance of each tracer which then lead to the estimation of soil ingestion detection limits of each tracer for studies performing mass-balance analyses. Based on these analyses it is concluded that the Binder et al. (1986) and Van Wijnen et al. *(1990) studies provide no convincing evidence to support qualitative and quantitative estimates of soil ingestion due to inherent limitations of their respective study designs. The Davis* et al. *(1990) and Calabrese et al. (1989) studies displayed convincing qualitative evidence of soil ingestion. However, the results indicate that the median soil ingestion estimates of Davis et al. were less reliable than those of Calabrese et al. The range of detection limits vary according to the tracer and the assumption of acceptable precision in recovery estimation. The minimum detection level of soil ingestion in children in the Calabrese* et al. *study with a variance in recovery of 100% ± 20% was 16 mg day^{-1} based on Zr.*

These findings are of particular regulatory significance since they provide: (1) a method of assessing the level of detection inherent in soil ingestion studies, (2) a reevaluation of the major soil ingestion studies in light of new methodology, and (3) guidance for future studies so that detection capacity can now be included in the presentation of study findings.

Introduction

Concern over ingestion of soil by humans, especially children, has become an area of regulatory concern. Estimation of soil consumption has strongly influenced risk assessment activities associated with dioxin contamination at Times Beach, Missouri (Kimbrough *et al.* 1984), as well as childhood lead risk assessments (NRC, 1980). Modern estimates of soil ingestion have been based on the use of soil tracer agents that ideally would be present in soil, not present in human foods and medications, and poorly absorbed via the GI tract. The use of soil tracer methods has represented a major improvement in the quantitative estimation of soil ingestion over previous qualitative and semi-quantitative estimates of soil ingestion (Kimbrough *et al.*, 1984; Lepow *et al.*, 1974; Day *et al.*, 1975). Four major soil tracer studies (Binder *et al.*, 1986; Calabrese *et al.*, 1989; Van Wijnen *et al.*, 1990; Davis *et al.*, 1990) and one pilot study (Clausing *et al.*, 1987) have now been completed and provide the basis of current estimates of soil ingestion in children. A striking observation is the remarkable interstudy consistency in the estimated soil ingestion values amongst these studies despite the fact that they were conducted by four different research teams, in three different parts of the USA and the Netherlands, involved different seasons of the year and a variety of different tracer elements (Table 1). This evaluation is designed to assess the capacity of soil tracer methodologies to derive reliable estimates of soil ingestion. Particular emphasis will be directed to the validation of the mass-balance methodology, selection of tracers, sensitivity of the method and the issue of negative values. In light of this assessment, the available studies will be examined to assess to what extent their individual and collective estimates of soil ingestion are reliable.

Background

The basic concept behind a soil tracer study is that the ingestion of an element from non-soil and soil equals the amount excreted in feces and urine. Soil intakes can be estimated by making measurements of tracer concentrations in ingested items (*e.g.* food, medications, vitamins, toothpaste), feces, and urine. Mathematical expression of the mass-balance relationship is provided in the previous paper (Stanek and Calabrese, 1991).

As noted above, an ideal tracer would be one that is poorly absorbed into systemic circulation, is not inhaled in appreciable amounts, and is present in ingestible items in only trace quantities. Unfortunately, many tracers are indeed present as

Table 1 *Soil ingestion estimates in children (mg day^{-1}).*

	Binder *et al.*		Van Wijnen *et al.*		Davies *et al.*		Calabrese *et al.*	
	Mean	Median	Mean	Median	Mean	Median	Mean	Media
Al	181	121	–	–	40	25	153	29
Si	184	136	–	–	82	59	154	40
Ti	1,834	618	–	–	246	81	218	55
Ba	–	–	–	–	–	–	32	<0
Mn	–	–	–	–	–	–	<0	<0
V	–	–	–	–	–	–	459	96
Y	–	–	–	–	–	–	85	9
Zr	–	–	–	–	–	–	21	16
Limiting tracer method (LTM)								
(Day care center)			103	111				
(Campers)			213	160				

minor constituents of foods or other ingestible products, and hence they must be accounted for in mass-balance studies (Stanek *et al.*, 1988).

Documentation of tracer intake needs to be included as a component of soil ingestion studies since it permits the identification and quantification of tracer elements from non-soil sources and helps prevent over-estimation of soil ingestion. For this reason, food collection (in the form of duplicate food samples or their surrogates) is an important component of soil ingestion studies. However, because of their high cost, the mass-balance component of soil ingestion studies has been of limited duration (3–5 days).

Despite its importance, collection of food and medication is not sufficient to eliminate food as a contributor to variability or bias in soil ingestion studies. Consequently, mass-balance studies of limited duration may not be able to achieve an adequate input-output equilibrium resulting in input-output misalignment. This results in both under and over-estimates of soil ingestion. For example, individuals consuming unusually high amounts of a tracer element from food on the day prior to a four-day mass-balance study may display extremely high levels of the tracer in their fecal sample over the next several days. This could lead to a gross over-estimate of soil ingestion.

The reverse situation could also occur, resulting in under-estimation of soil ingestion. If variation in food consumption of the tracer elements were negligible from day to day, the magnitude of soil ingestion error due to food/fecal sample misalignment (both under and over estimations) would be quite small. The quantitative implications of misalignment error is the requirement that negative estimates of soil ingestion be included as negative values in order to cancel out positive error estimates, even though it is not possible to ingest negative amounts of soil. If one were to count the negative values as zero it would leave the positive over-estimates in place and would retain an over-estimation error. We first briefly review the study design of individual soil ingestion studies. Since three studies have important methodologic limitations (Binder, Clausing and Van Wijnen), such limitations will be discussed in the . of each study. For the two remaining studies (Calabre Davis) we briefly review the individual study's metho and then attempt to critically evaluate these studies resu

Specific Studies

Binder et al., *1986*

This study collected fecal samples on 59 children 1–3 y age over a three day period. Soil and dust samples we obtained from the residences of the children but no foc collected. The soil tracer elements employed were Al, Ti.

The Binder *et al.* study was an important effort s represented the first attempt to provide a quantitative st estimate soil ingestion. However, a major limitation of the was the lack of intake measures contributed from food and non-soil sources. In addition, the Binder *et al.* study assumed that the amount of fecal matter excreted was greater than measured in their study (15 g *vs* 7.5 g of dried fecal matter). This was to compensate for what believed to be a sample loss in their study.

By not taking food into account, the Binder *et al.* provided at best an upper bound estimate of soil ing assuming all fecal tracer quantities came from ingested so impact of using 15 g freeze dried fecal weights on soil ing estimates is to double estimates relative to comparable est based on observed fecal weights. Unfortunately, the stud unable to quantify fecal sample loss, so soil ingestion est are directly dependent on the assumed 50% fecal s collection.

Clausing et al., *1987/Van Wijnen* et al., *1990*

These two studies followed the same basic approach as B *et al.* in that soil tracers were employed to estimat ingestion. However, the studies differed from the Binder methodology in several important respects. First, the u

used were Al, Ti and acid insoluble residue (AIR). The AIR feature was used since the investigators were unable to adequately solubilize Si. Second, like the Binder *et al.* study, no food was collected from the free-living subjects and thus no mass-balance approach was used. However, to compensate for this limitation the investigators employed what they termed a hospital control group that was assumed not to have ingested tracer containing soil or dust. Duplicate samples of the hospital controls' food were analyzed for each tracer. The amounts/concentrations of tracers in the food of the hospitalized subjects were assumed to be the same for each of the non-hospitalized subjects and subtracted from their fecal tracer total.

The Van Wijnen *et al.* study also used the lowest of the three tracer values to estimate soil ingestion (*i.e.* limiting tracer method, LTM) since they claimed that the lowest value could not be logically exceeded. The collection of total daily fecal samples was likely to be considerably less than complete since entry into the study was permitted with a single fecal sample with further daily follow-up for other possible fecal samples not rigorously pursued. To compensate for possible uncollected or lost sample material they assumed that each individual produced a daily fecal value of 15 g of freeze dried sample and adjusted excreted tracer values accordingly. The Van Wijnen *et al.* study evaluated 292 subjects ranging in age from 1–5 years. The children involved individuals residing in suburban and urban settings, as well as children on camping vacations.

The Van Wijnen *et al.* protocol possesses several methodological limitations which affect the interpretation of the study. The use of hospital controls to assess food tracer intake by all subjects represents an improvement over the Binder *et al.* report. However, it is questionable that the hospitalized children's food intake is representative of the non-hospitalized subjects' food intake. This question, which is critical to the validity of the report, was not specifically evaluated by Van Wijnen *et al.* It may be speculated that hospitalized children are more likely to be less physically active, have lower caloric requirements, consume less food and therefore, have different and probably less food tracer intake than free-living children. In addition, the range of food items in a hospital would most likely be far less variable than in free living families. This is supported by the Van Wijnen *et al.* data that demonstrated little interindividual variability (1.7-fold for the 95% confidence interval) in LTM values in hospitalized children. The implication of these two factors is that the total tracer quantity ingested by free-living children may be significantly under-estimated and therefore soil ingestion may be over-estimated for such children. The soil ingestion estimates are also likely to have artificially high variability due to the assumption of constant food ingestion between subjects. These data emphasize the critical need to clarify how well the hospitalized controls in the Van Wijnen *et al.* study represented the tracer consumption patterns of free-living children in order to estimate the potential bias in the soil ingestion estimates for children.

The Van Wijnen study made no effort to assure total daily fecal collections and specimens were scaled up to 15 grams of dried feces per day. For example, if a daily sample had 5 g, it was assumed the child excreted 15 g day^{-1} and that fecal tracer concentration would remain constant. In such a case the tracer value was increased by a factor of 3 to adjust for the 'lost' fecal weight. As in the Binder study, the arbitrary use of 15 g day^{-1} fecal weight may severely bias estimates of soil ingestion values.

A final limitation of the Van Wijnen study is the use of the least tracer method (LTM) in estimating soil ingestion. The least tracer method appears to have no biologically based foundation inherently supported by the tracer methodology employed and is likely to result in an under-estimate of soil ingestion. Selection of the best tracer is not based on which tracer provides the lowest values, but more appropriately the one that is established through proper validation. Issues such as tracer recovery values, tracer intake variability, transit times, food/soil ratios and gastrointestinal absorption efficiency, should be addressed when determining which tracer(s) provides the most reliable estimate of soil ingestion.

In summary, the lack of a validated mass-balance approach, the use of a hospital-based control without reference to its representiveness to free-living children, and the use of fecal sample size scale up procedures, limit the ability of the Van Wijnen *et al.* study to reliably quantify soil ingestion in children.

Calabrese et al., *1989*

The third major study on soil ingestion in children (n = 64) was that of Calabrese *et al.* (1989). This study, which followed the basic tracer design of Binder *et al.*, added several methodological improvements to the previous studies. These included the use of a mass-balance methodology study over a two week period in which duplicate samples of food, medicines, vitamins, *etc.* were collected and analyzed on a daily basis. In addition, this study attempted to validate the mass-balance methodology used with the children by administering known amounts of soil to adults using eight tracer elements (Al, Si, Ti, Ba, Mn, V, Y, Zr).

The validation study established that a four-day mass-balance protocol was able to quantitatively estimate the amount of soil ingested by adults at a daily rate of 500 mg day^{-1}. Less reliable but still acceptable tracer recoveries were obtained when the subjects were administered 100 mg of soil per day. This validation study not only confirmed that the methodology could quantitatively estimate soil ingestion but it also provided information on which elements had the potential to be the most reliable tracers. Calabrese *et al.* (1989) concluded that when food intake was not accounted for in the mass-balance approach, estimated soil ingestion values would have been higher by several fold depending on the specific tracer.

Davis et al., *1990*

A recent report by Davis *et al.* (1990) used Al, Si and Ti as the tracer elements in a four day mass-balance study that included measurements of the tracers in food, feces and urine as a one week average value. Since daily samples were not analyzed, daily variation in tracer input/output could not be assessed. This study was based on observations on a random sample of 104 2–7 year-old children. Children in diapers were excluded from the study. This study also addressed medicines and vitamins ingested as was done in the Calabrese *et al.* study. No validation of their study protocol was attempted.

Qualitative Evidence that Children Ingest Soil

An essential feature of the results of soil ingestion studies using a mass-balance methodology as noted above is that subjects can be observed as displaying either positive or negative soil ingestion values. While negative soil ingestion can not actually occur, the mass-balance approach can yield negative soil ingestion estimates. This is an important artifact of mass-balance studies that occurs when food intake and fecal output measures are somewhat out of proper alignment. Qualitative evidence of soil ingestion is indicated when the proportion of positive soil ingestion estimates exceed the proportion of negative soil ingestion estimates.

With the above information as a background, the following tracers had negative soil ingestion values in a sizeable percentage of subjects in the Calabrese *et al.* report: Al 14%, Si 25%, Ti 30%, V 13%, Y 44%, and Zr 36%. Similarly, the Davis *et al.* report had negative soil ingestion estimates for Al 12%, Si 32%, and Ti 25%. While even under ideal mass-balance conditions negative values would not be unexpected, there is little question that in each study some degree of input and output misalignment occurred.

Negative soil ingestion estimates would be expected to occur more frequently for tracer elements with high food-to-soil ingestion ratios. This is supported in an adult validation study (Calabrese *et al.* 1990). When study subjects were administered 100 mg day^{-1} of soil, seven negative ingestion values were reported out of 48. No negative soil ingestion estimates were reported when the subjects were administered 500 mg day^{-1} of soil. Furthermore, the tracer elements Ba, Mn and Ti which showed high food-to-soil tracer ratios of > 10.0 in the 100 mg day^{-1} study of the adult study each had two instances out of six with negative soil ingestion estimates (Table 2).

Even though sizeable percentages of negative values exist, this would not be an argument against soil ingestion unless > 50% of the subjects displayed negative values. The fact that the positive soil ingestion estimates occur from 56 to 88% of the time depending on the tracer in the Calabrese *et al.* (1989) study and 68 to 88% of the time in the Davis *et al.* report argues strongly that soil ingestion is occurring. Despite this circumstantial evidence to support soil ingestion, is it possible to explain the presence of tracers in fecal matter of the children by foods, medicines, *etc.*, and not by consumption of soil?

The ability of tracers in foods, toothpaste and medicines to mask true soil ingestion can be evaluated through comparison of the relative contributions of each to the fecal output. Table 3 shows the median tracer values for fecal output and food intake as well as the potential contribution of toothpaste to the tracer intake of the children in the Calabrese *et al.* (1989) study.

The median value of tracer excreted in feces for the children is presented in column 1 of Table 3. The median daily amount of tracer ingested from food is given in Column 2. Toothpaste ingestion estimates for three elements in Column 4 are based upon a study by Barnhart *et al.* (1974). The total tracer amount ingested is given in Column 5.

The data indicate that Al, Ti, V and Zr have more tracer element quantity in fecal samples than can be accounted for by food ingestion. In contrast, Si, Ba and Mn are in negative balance while Y input and output were equivalent. These data suggest that food ingestion and toothpaste cannot account for the presence of all the tracer amounts found in the feces for Al, Ti, V, and Zr. However, it should be emphasized that the e positive excretory balance of Si can be accounted for ingestion of toothpaste without regard to the need for emplo soil ingestion. This has considerable relevance to each of published soil ingestion studies. Thus, unless a non-sili toothpaste were employed, the utility of silicon as a tracer children is severely compromised. This will not be the case adults where toothpaste ingestion has been reported to negligible (Barnhart *et al.*, 1974). With respect to the use of as a tracer, it appears that toothpaste ingestion may account up to about 30–100% of the excess Al tracer in feces assum they brush their teeth from once every other day, up to two ti a day, and may therefore nearly fully account for the pos fecal Al balance.

In summary, it may be reasonably concluded t qualitative evidence exists that children ingest soil. The cru issue for the perspective of possible risk assessment practic the quantification of ingestion estimates.

Quantitative Estimates of Soil Ingestion In Children

A critical issue in quantifying soil ingestion is the reliabilit soil ingestion estimates within the context of the mass-bala methodology. Only one validation study has been conducted the mass-balance methodology for estimating the quantity soil ingested; the methods were validated among six a volunteers over a three week period (Calabrese *et al.*, 19 This study assessed whether the methodology could determ the amount of soil ingested when the volunteers w administered either 100 or 500 mg of soil per day for three d Direct validation of the methodology among children is m difficult, in part due to difficulties in getting informed cons as well as due to the relatively high soil dose levels needed. a result, quantitative estimates of soil ingestion in children dependent upon the assumption that the mass-bala methodology is valid, including its extrapolation from the a validation study.

Four major assumptions are necessary for extrapolation of the tracer findings from the adult stud children's studies. First, the GI transit times are assumed t comparable between adults and children. Second, absorption efficiencies are assumed to be comparable betw adults and children. Third, the food to soil tracer ingestion ra are assumed to have a similar range between children adults; fourth, the variation in daily tracer ingestion is sim between children and adults.

Table 2 provides information on tracer recovery in adult validation study. The results clearly indicated that A and Y were the most reliable tracers at the 500 mg day^{-1} l based on their approximately of 100% recovery and the sma variability as measured by the standard deviation (SD) o mean. The findings were not nearly as clear at the 100 mg d intake rate. At the ingestion rate of soil of 100 mg day^{-1} per recovery deteriorated. Al, Si, and especially Y and Zr appe to be the most reliable tracers. For those tracers, reco percents ranged from 80–153% while the SD refle considerably greater variation than at the 500 mg day^{-1} l The recovery study indicated that with $n = 6$, the mass-bal method reliably confirmed the ingestion of 500 mg day^{-1} o with acceptable variability (1SD<20%). However, at the l soil ingestion level (*i.e.* 100 mg day^{-1}) the recovery of soi

Table 2 *Percent recovery of eight tracer elements in adult validation study.*

ID	Ba	Mn	Si	Al	Ti	V	Y	Zr
100 mg day^{-1} of soil ingestion								
0966	361	1,150	88.9	86.0	105	693	108	28.4
0967	0	0	0	70.0	0	99.1	94.4	35.5
0968	11,500	0	101	96.1	522	260	118	89.6
0969	1,373	3,320	431	301	762	527	205	146
0970	592	2,190	133	281	120	67.9	92.6	101
0971	0	403	81.7	82.8	0	423	105	83.0
Mean	2,300	1,180	139	153	252	345	121	80.6
SD	4,530	1,340	150	108	316	247	42.4	43.7
500 mg day^{-1} of soil ingestion								
0966	179	187	84.8	92.9	337	245	99.4	63.2
0967	168	201	81.7	91.2	25.3	178	87.2	32.2
0968	95.7	234	94.6	108	139	116	84.2	58.6
0969	258	613	120	107	92.8	179	102	6.6
0970	139	120	97.6	96.5	93.8	114	66.7	61.1
0971	59.3	135	72.0	65.4	1,030	53.8	85.5	106
Mean	150	248	91.8	93.5	286	148	87.5	54.6
SD	69.5	184	16.6	15.5	380	66.8	12.6	33.4

Note: 0% recovery corresponds to a negative soil ingestion estimate.

highly variable (1SD>40%). Thus, by lowering the daily soil ingestion rate from 500 to 100 mg day^{-1} precision was diminished and variability was markedly enhanced. The adult validation data suggest that much less confidence exists with respect to the 100 mg day^{-1} soil ingestion estimates. Despite this greater statistical uncertainty, it is still reasonable at least for Y and Zr to conclude that soil ingestion could account for the enhanced presence of tracers in the feces both qualitatively and quantitatively among the adults.

These findings suggest that tracers (*i.e.* Y and Zr) not previously employed in any other study may be the most reliable for soil ingestion estimates. Additionally, the tracer Ti which has featured prominently in the Binder *et al.*, Clausing *et al.*, and Davis *et al.* studies, yielded poor average recovery values in the adult validation study. Definitive conclusions concerning Ti are not possible in the adult study due to the small sample size (and unusually high recovery estimate for ID 0971 at the 500 mg day^{-1} level), but the relatively poorer recovery results at both the 100 and 500 mg levels suggests that Ti is not the best element for the mass-balance approach based on the adult study.

Al and Si which performed quite well with respect to recovery efficiency at 500 mg day^{-1} were at best only marginally acceptable at 100 mg day^{-1}. In fact, the adult validation study results call into question the ability of the Binder *et al.* Clausing *et al.*, Davis *et al.* studies for providing reliable estimates of soil ingestion for children. Their conclusions about soil ingestion estimates are made even more questionable by the further concern that if Ti as well as Al and Si are inadequate in the validation method at soil ingestion rates of 100 mg day^{-1}, it is expected that they become even less reliable at lower levels of estimated exposure.

In order to evaluate the extent to which estimates become unreliable at low soil ingestion rates, the companion paper in this issue of the journal developed a biomathematical model to estimate the capacity of soil ingestion studies to measure the precision of soil recovery. By determining the precision of soil recovery the model established the foundation by which a minimal capacity to detect soil ingestion in subjects may be made. The analysis indicated that the primary factors affecting the capacity to estimate minimal soil ingestion detection of a study are the food to soil tracer ingestion ratios and the sample size of the study.

To date none of the published studies on soil ingestion have addressed the capacity of their particular study to detect soil ingestion. It has been tacitly assumed that what was calculated to be estimates of soil ingestion were in fact able to be reliably measured by the study. The model indicates that this is an erroneous assumption and provides a vehicle by which the soil ingestion detection levels may be estimated both prospectively and retrospectively. Consequently, we now apply the developed model to determine whether the published studies on soil ingestion were actually able to detect the soil ingestion levels they published and at what level of precision. Since only the Calabrese *et al.* (1989) and Davis *et al.* (1990) studies performed mass-balance studies on their subjects, they are the only studies that can be directly re-assessed by the model. Table 4 provides an application of the model to both studies. It indicates the level of precision with which various soil estimates could be made for each tracer.

The data indicate that considerable inter-tracer variability exists with respect to the degree of tracer precision at various soil ingestion levels. Table 4 repeats the median values given in the Calabrese *et al.* and Davies *et al.* studies. The data for

Table 3 *Comparison of median daily fecal output and food intake tracer values of 64 children in the Calabrese* et al. *study.*

Element	Median daily[a] fecal output Column 1	Median daily[b] food ingested Column 2	Ratios of columns 1:2 Column 3	Estimated* toothpaste daily total Column 4	Median summation of columns 2:4 Column 5	Median difference columns 1–5 Column 6
Al (mg)	2.8	1.21	2.31	0.5	1.7	+ 1.09
Si (mg)	24.6	14.2	1.73	24.3	38.5	- 13.9
Ti (mg)	0.58	0.20	2.90	0.01	0.21	+ 0.37
Ba (μg)	199	224	0.888	NA	224	- 25.0
Mn (μg)	975	1,288	0.757	NA	1,288	- 313.0
V (μg)	12.6	5.3	2.38	NA	5.3	+ 7.3
Y (μg)	1.12	1.1	1.02	NA	1.1	0.02
Zr (μg)	5.7	2.5	2.28	NA	2.5	+ 3.2

[a] Calabrese *et al.*, 1989, Table 7, Chapter 30, p.375.
[b] Calabrese *et al.*, 1989, Table 10, Chapter 30, p.377.
* 1 brushing every other day.
NA = not available.

Table 4 *Approximate 95% confidence interval estimates for soil ingestion (mg day^{-1}) in children based on percent variance estimates and food/soil element concentrations.*

Study (A)	Element	*n*	Median	95% CI Using median of mean food	95% CI Using median of median food	1* Using median of mean food	1* Using median of median food	2* Using median of mean food	2* Using median of median food	Mean	
Calabrese	Al	128	29	(16,42)	(18,40)	45	37	107	77	153	
Calabrese	Si	128	40	(17,63)	(19,61) 9	57	52	219	191	154	
Calabrese	Ti	128	55	(25,85)	(43,67)	55	22	284	64	218	
Calabrese	V	128	96	(50,142)	(49,143)	48	49	400	418	459	
Calabrese	Y	128	9	(0,22)	(0,21)	145	134	228	199	85	
Calabrese	Zr	128	16	(8,24)	(13,19)	47	20	65	16	21	
Calabrese	Al	64	29	(11,47)	(14,44)	63	52	188	136	153	
Calabrese	Si	64	40	(8,72)	(10,70)	80	74	385	336	154	
Calabrese	Ti	64	55	(12,98)	(38,72)	77	31	500	113	218	
Calabrese	V	64	96	(31,161)	(29,163)	68	70	703	735	459	
Calabrese	Y	64	9	(0,27)	(0,26)	205	189	401	350	85	
Calabrese	Zr	64	16	(5,27)	(11,21)	67	28	114	28	21	
Davis	Al	101	25	(0,57)	NA	125	NA	501	NA	40	
Davis	Si	101	59	(21,98)	NA	65	NA	407	NA	82	
Davis	Ti	101	81	(22,139)	NA	72	NA	652	NA	246	

1* Variation in percent recovery of soil tracers at the median value for soil ingestion. This column should be read as follows. the case of Al for the Calabrese *et al.* study assuming 29 mg of soil were ingested based on Al as the tracer, the chemical analytical procedures were able to recovery 100% ± 45% (representing 2 SE).
2* Median amount of soil ingestion (mg day^{-1}) required to have a percentage recovery of 100% ± 20% (representing 2 SE).
NA = not available

Calabrese *et al.* are provided when the unit of analysis is the total number of subjects (n = 64) or the number of subject weeks (n = 128). Statistical analyses reported in the model development paper have indicated that subject effects were minimal or absent in these data, so that each weekly unit of observation can be considered as an independent observation. This implies that using n = 128 is the best estimate of relevant sample size. However, for completeness and recognition of possible alternate interpretations we ha included data analysis if the unit of analysis were the subj (*i.e.* n = 64).

Based on the soil recovery variance model in Stanek a

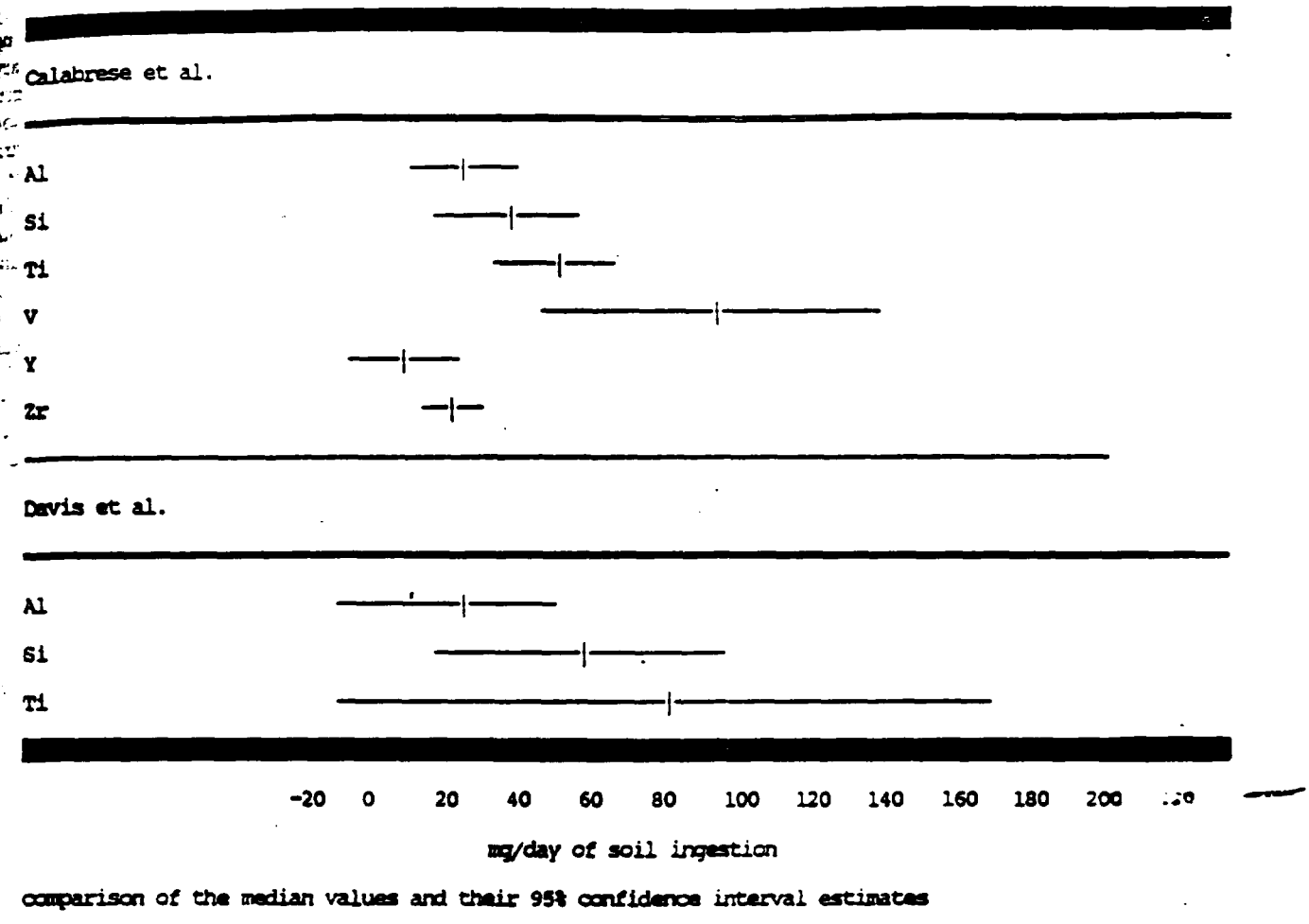

Figure 1 *Distribution of median soil ingestion estimated in the Calabrese* et al. *and Davis* et al. *studies*

Calabrese (1991), lower and upper 95% confidence interval estimates of the median and mean were calculated. Column 1* provides an estimate of the variation in percent recovery of soil ingested tracers at the median value for soil ingestion. Column 2* provides the median value of soil ingestion by tracer required to be ingested in the Calabrese *et al.* and Davis *et al.* studies in order to achieve a tracer recovery with a 95% confidence interval of 100% ± 20%, a number selected because it represents a marginally acceptable recovery value. It is calculated using equation 3 of Stanek and Calabrese (1991).

The key issues surround interpretation of this table. Different interpretations may result, depending upon whether the results are approached from a biostatistical and analytical chemical framework. While these interpretations should not be in conflict with each other, they perceive the data from distinctly different paradigms and both need to be understood and considered. Each is worthy of separate consideration.

Statistical Interpretation

We first discuss how this table would be interpreted within a biostatistical framework. As an example, consider interpretation of the confidence interval for the median value of Ti from the Davis *et al.* study. The median soil ingestion estimate for this sample of 101 subjects was 81 mg day^{-1}. If the true median soil ingestion for this population was 81 mg day^{-1}, [illegible] population were re-sampled 100 times (say on different [illegible] or with different subjects) then we could expect 95 of the 100 median soil ingestion estimates to fall between 22 and 139 mg day^{-1}. The broad range of the CI indicates low confidence in the median of 81. Clearly, it is most desirable to focus on a tracer than had a median value with a narrow confidence interval. The narrowest CI for median soil ingestion is from Zr in the Calabrese *et al.* study, where the median is 16 and the 95% confidence interval is 8–24 mg day^{-1}.

From a statistical perspective those tracer elements with the smallest confidence interval estimates (expressed as a percent of the estimated median) are considered superior to those with larger confidence intervals. This criteria selects Al, Si, Ti, V, and Zr of the Calabrese *et al.* study and Si, and Ti of the Davis *et al.* study as tracers with the lowest 95% confidence interval.

These five tracer elements produce median estimates of soil ingestion in two populations. These estimates range from 16–96 mg day^{-1}. One would hope that their distribution would have a strong degree of overlap since this would support the assumption of inter-tracer reliability. Figure 1 illustrates that considerable overlap exists for Al, Si, Ti, and Zr. However, there is no over lap between Y and Ti, Zr and Ti, and V and Y. This lack of inter-tracer reliability is troublesome since they are

describing the same population. Nonetheless, the range of median values covered by confidence intervals for the five tracers with the smallest relative variance is from 0 to 142 mg day^{-1}.

Analytical Chemistry Interpretation

The issue of recoverability of ingested soil via the tracer elements is crucial to the estimation of soil ingestion rates. It has been established in the Calabrese *et al.* (1989) adult soil ingestion study that high variability in the recovery study was associated with high food-to-soil ratios, and that this observation became an integral component of the predictive equation for estimating the confidence interval for soil ingestion.

As with the statistical framework, consider the Davis *et al.* study again and the Ti tracer element from an analytic perspective. Table 4 indicates that at the median ingestion rate of 81 mg day^{-1} an estimated 95% CI for percent recovery based on Ti would be 100% ± 72%. This type of performance in recovery studies would generally be considered highly unreliable and not acceptable. In order to achieve a marginally acceptable value of 100% recovery ± 20%, the amount of soil ingestion would have to be 652 mg day^{-1}. Thus, from a chemist's perspective the median value of 81 mg day^{-1} for Ti in the Davis *et al.* study could not have been reliably recovered. This is also true for Al in the Davis *et al.* study which also had a large variance in percent recovery.

The recovery value for Si in the Davis *et al.* (1990) study is 100% ± 65%. However, when adjustment is made for the ingestion of silicon in toothpaste which was attributed to the fecal sample (as soil ingestion) and not counted as food, not only does the estimated amount of soil ingestion decrease by 45% from 59 mg day^{-1} to 37 mg day^{-1} but the precision in the recovery of silicon would become markedly less because of higher food to soil ratios. If the three tracers used by Davis *et al.* were to achieve a recovery of 100% ± 20% (a marginally acceptable standard for recovery in mass-balance studies, with 20% representing 2 SD) the median level would have had to be 501 g of soil ingested based on Al, 407 mg of soil based on Si (the uncorrected value) and 652 mg of soil based on Ti. In effect one could view this as establishing a level of soil ingestion detection for tracer elements in the study. The view of the analytical chemist would be that the values of 25 (Al), 59 (Si), and 81 (Ti) mg day^{-1} that Davis *et al.* estimated for soil ingestion could not be reliably seen and were considerably below the minimum level of detection for soil ingestion in the study.

The analysis of the Calabrese *et al.* (1989) data examined two different methodological approaches for the derivation of a soil ingestion detection level. One was based on analysis of food tracer ingestion values that were estimated as the median of 64 children. Within this context, each individual child's average tracer ingestion value represented the mean of their six daily values (three per week for two weeks). Thus, the summated value represented a median of the mean value. The second approach again represented a median value of the 64 children. However, in this case, each individual child's value represented the median of their six daily values. Thus, the summated value represented the median of the median. The selection of which approach to use is critical since for some tracers such as Ti and Zr the estimated soil ingestion detection values differ by a of four or more (Table 4, compare the two columns unde For the other tracers the differences between the two appro are relatively minor. The lack of agreement amongst th approaches for Ti and Zr are the result of a more log n distribution of tracer ingestion for these two trace individual subjects. Since our intent is to utilize the measure of central tendency of the study population, the m of the median was selected. Nevertheless, the results o approaches are provided. Table 4 reveals that Zr and T ingestion estimates of 16 and 55 mg day^{-1} were seen precision of 100% ± 20% and, 100% ± 22%, respectivel third best tracer, Al, with a median soil ingestion value mg day^{-1} was seen with a precision of 100% ± 37%. T achieved a 100% ± 20% recovery value for Al the s would have needed to ingest 77 mg day^{-1} of soil (*i.e.* le acceptable soil ingestion detection) using the median median approach.

As noted above, using the median of the mean ap would have a profound impact on the detection of soil ing for Zr and Ti (*i.e.* decreasing sensitivity by greater than 4 while having only a modest (~30%) impact with Al. S modification in statistical methodology can lead to eno changes in the conclusions of a study. However, regard which approach is selected, Zr was the most reliable trac a soil ingestion detection value of 16 mg day^{-1} (median median method) versus 65 mg day^{-1} (median of the me

It is useful to directly compare the minimum le detection values for each tracer based on different p recovery levels. For example, if the recovery value increased from 100% ± 20 % to 100% ± 40% the soil de limit would become more sensitive (*i.e.* decrease) by a fa about 3.1. That is, the 65 mg day^{-1} (median of the mean for Zr in the Calabrese *et al.* (1989) study value would de to 21 mg day^{-1}. On the other hand, if the recovery selected was 100% ± 10% the detection value based would jump to 202 mg day^{-1}.

The results of this analysis need to be placed in a b perspective. It was initially thought that since ther considerable interstudy agreement concerning soil ing values amongst children that this strongly suggested tha should be a high degree of confidence in the overall g findings. However, the present analysis has challenged n the methodological basis of the Binder *et al.* (1987) ar Wijnen *et al.* (1990) reports, it argues that reported val soil ingestion of Davis *et al.* (1990) were far below the of detection and that this was also the case for six of th tracers in the original Calabrese *et al.* (1989) report. Th present analysis has called into question a considerable of the soil ingestion data base that has been widely u regulatory/risk assessment professionals. Despite this a erosion of the quantitative data base, the present study of the first time the means to assess the soil detection ca of such studies with a specific degree of precision. Th believe that the present analysis provides for a me assessing not only the soil ingestion detection capabi also the degree of confidence in that value. Within this it is important to point out that the soil ingestion value and Ti in the Calabrese *et al.* (1989) of 16 and 55 mg respectively, were able to be detected at approxi 100% ± 20% and thus achieved acceptable norms.

General Conclusions

(1) The soil tracer methodology incorporating a mass-balance approach can be employed to reliably estimate soil ingestion.
(2) Further studies are needed to validate the methods to the extent possible in the population being tested.
(3) Adult validation studies may not yield accurate determinations of what is an ideal tracer in children studies due to differences in food intake and transit time.
(4) A low food-to-soil tracer ingestion ratio predictive method is a useful tool for estimating the soil ingestion detection limits of specific studies.
(5) Further studies of soil ingestion are warranted with adequate power, design and tracer selection to quantify soil ingestion in children.
(6) Further experimental studies with capsule doses are warranted to characterize the food/capsule tracer relationship.
(7) Inconsistencies between tracer results still continue to exist, and warrant further investigation.

Specific Conclusions

(1) The estimates of soil ingestion by Binder *et al.* and Clausing/Van Wijnen *et al.* are of unknown reliability and cannot be accepted because of methodological limitations.
(2) Qualitative evidence of soil ingestion is provided by the Calabrese *et al.* (1989) and Davis *et al.* (1990) study.
(3) Selection of ideal tracers for children based on the adult validation study proved problematical since the food-to-soil tracer ingestion ratios varied markedly for some tracers (*e.g.* Ti). This accounted for the poor recovery of Ti in the adult study and the improved precision for Ti recovery in the children study.
(4) The original median estimates of soil ingestion by children in the Calabrese *et al.* (1989) study and Davis *et al.* study need to be interpreted within the context of the soil ingestion detection level of the study. Within this context the median soil ingestion values based on Al, Si and Ti of Davis *et al.* (1990) were below an acceptable estimated level of detection for soil ingestion. Of the eight tracer-based soil ingestion estimates of Calabrese *et al.* (1989) Zr, Ti and possibly Al were detected with an acceptable estimated precision of recovery and thus provided a reliable quantitative estimate of median soil ingestion rates in the studied population. Values of 25(Al), 59 (Si), and 81 (Ti) mg day^{-1} that Davis *et al.* estimated could not be reliably seen and were considerably below the level of detection for soil ingestion in that study. Of the eight tracer-based soil ingestion estimates provided by Calabrese *et al.* (1989) Zr and Ti and possibly Al were detected with an acceptable precision of recovery and thus provide a reliable quantitative estimate of soil ingestion in the studied population.
(5) Published soil ingestion estimates for adults by Calabrese *et al.* (1990) were below the soil ingestion detection capability based on the application of the model presented here. The minimum detection levels of soil ingestion for adults in that study were 224 mg day^{-1} based on Zr, and 374 mg day^{-1} based on Al. The data from the adult study needs to be interpreted in this light (see Stanek and Calabrese, 1991).

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Methodological Considerations in Soil Ingestion Estimation

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Abstract

Methodological considerations play an important role in forming population estimates of soil ingestion in children. Two important areas of controversy are the hypothesized log-normal distribution of ingested soil and the identification and appropriateness of methods for handling outliers. Each of these issues is discussed in the context of data collected on soil ingestion in Amherst, Massachusetts. Non-parametric methods are recommended as most suitable and appropriate for analysis of soil ingestion studies.

Introduction

Estimates of casual soil ingestion in a free living population have important regulatory, public health, and fiscal significance. Due to their anticipated higher risk, most soil ingestion estimates have been made among young children. Since soil ingestion estimates for children are skewed to the right and some estimates may be exceptionally large, different methodological approaches may be adopted to summarize soil ingestion.

One common assumption is that soil ingestion is log-normally distributed. If this assumption is valid, the logarithm of soil ingestion is normally distributed. This implies that:

(1) The mean and median of the log-normal distribution will be the same.

(2). Confidence intervals constructed for the log-normal distribution can be exponentiated to generate confidence intervals on the natural scale.

(3) Hypotheses can be tested in the usual way using appropriate comparison distributions.

A second issue relates to how to handle exceptionally large or unusual soil ingestion estimates. Some investigators exclude such estimates when summarizing soil ingestion, while others argue that all data should be included.

The purpose of this paper is to review the evidence for the log-normal distribution of soil ingestion, and discuss the implications of exceptionally large values using data from a large scale soil ingestion study on pre-school children. In so doing, some technical issues relevant to the mass-balance approach for estimating soil ingestion will be discussed. This note was prompted by a reviewer's comments suggesting adoption of alternative methodological approaches when analyzing soil ingestion data. Since the issues raised by the reviewer may be concerns shared by others, we felt a discussion of these issues warranted broader dissemination.

Materials

To evaluate the appropriateness of various approaches to summarize soil ingestion data, we use data from a University of Massachusetts study on 64 pre-school children [illegible] over a two-week period in 1986 (Calabrese *et al.* 1989). Briefly, children recruited from day-care centers were followed for two weeks, with duplicate food samples and fecal and urine collected from each child during this period. Eight trace elements (Al, Ba, Mn, Si, Ti, V, Y, and Zr) were measured in the input (food) and output (fecal samples and urine), and in the surrounding soil and household dust. A mass balance equation was used to estimate soil ingestion for each child in each week. Further details on the study design and results are given elsewhere (Calabrese *et al.*, 1989). We use these data to examine the appropriateness of various methodological approaches in soil ingestion analysis.

Results

The results of the UMass soil ingestion study clearly indicate that soil ingestion is skewed to the right and not normally distributed (Calabrese *et al.*, 1989). In the hope of making the soil ingestion distribution more normal, some investigators may use a log (base e) transformation. There are two potential problems with the log transformation. First, due to food input/fecal-urine output variability, some soil ingestion estimates are negative, and can not directly be used in a log transformation. The second problem is that the log (soil ingestion) may not be normally distributed.

A simple solution to the first problem is to add a constant to the soil ingestion estimate (making it positive), then take the logarithm, form an average, exponentiate the result, and subsequently subtract the constant. To evaluate how this proposed solution might affect soil ingestion estimates, we

† Special issue incorporating the Proceedings of [illegible]

Table 1 *Estimates of soil ingestion (mg day^{-1}) (number of subjects) based on the exponentiated geometric mean, after adding and later subtracting a constant.*

Consant added	Element Al	Ba	Mn	Si	Ti	V	Y	Zr
*	29 (64)	-36 (64)	-261 (64)	40 (64)	55 (64)	96 (64)	9 (64)	16 (64)
0	37 (55)	140 (28)	384 (18)	53 (49)	93 (45)	132 (56)	31 (37)	28 (41)
10 mg	36 (59)	108 (31)	202 (19)	54 (53)	117 (47)	148 (57)	28 (41)	20 (48)
100 mg	42 (64)	50 (40)	191 (23)	54 (64)	129 (53)	192 (58)	6 (60)	14 (60)
1 g	78 (64)	-20 (63)	-203 (52)	94 (64)	117 (62)	278 (62)	34 (61)	3 (62)
10 g	128 (64)	-9 (64)	-364 (64)	136 (64)	164 (64)	417 (62)	57 (62)	19 (62)

* Simple median including negative soil ingestion estimates.

considered addition of several constants and evaluated their effect on the mean soil ingestion. The results are given in Table 1 for the eight elements.

The results clearly suggest that this strategy of adding a constant prior to taking the logarithm does increase the number of subjects whose estimates of soil ingestion are positive, and can be included in the analysis. Two observations can be made of the effect of addition of a constant from Table 1. First, only addition of a large constant (1 g day^{-1}) will ensure all subjects are included in the analysis. Second, addition of the constant will produce biased estimates, with the direction of the bias depending on the element. The direction of the bias can best be judged by patterns in estimates with increasing constants, and comparison with an unbiased estimate (given by the median in the first row of Table 1). Addition of larger constants appears to have a positive biasing effect for Al, Si, Ti, and V, and a negative biasing effect for Ba and Mn. The strategy of addition of a positive constant to avoid negative estimates may be a standard practice. The results of Table 1 indicate that it is not an advisable one.

An alternative solution to the negative estimate problem may be considered by some investigators. This second approach uses a lower bound for soil ingestion (such as 0.1 mg day^{-1}) and analyzes the data as if they were censored. However, use of the method requires the assumption that soil ingestion estimates are log-normally distributed, since a distributional assumption is required to assess the degree of censoring. An examination of this assumption below indicates low confidence in the log-normal assumption. As a result, there appears no simple solution to the problem of negative estimates when using a log-normal distribution.

The second problem with the assumption that soil ingestion estimates are log-normal is that the estimates may not follow that distribution. Because soil ingestion estimates are skewed to the right, some investigators may assume that log (soil ingestion) is normally distributed. Shapiro Wilks tests for normality were performed for estimates of log (soil ingestion), based on adding a variety of constants. The results are summarized in Table 2.

The results indicate that soil ingestion may be log-normally distributed for some elements, and not for others. Although it is possible for estimates of soil ingestion based on different tracers to follow different distributions, true soil ingestion has a single distribution. The conflicting results for

Table 2 *p-Values for a test of normality (Shapiro–Wilks test) for soil ingestion estimates after adding a constant and then taking the logarithm by element and constant.*

Element	Constant added to soil estimate (g day^{-1}) 0.010	0.100	1.0	10.0
Al	0.0069	0.0001	0.0001	0.0001
Ba	0.0182	0.0022	0.0001	0.0001
Mn	0.0732	NS	0.0050	0.0001
Si	NS	0.0001	0.0001	0.0001
Ti	NS	0.0023	0.0001	0.0001
V	NS	0.0002	0.0001	0.0001
Y	0.0001	0.0001	0.0001	0.0001
Zr	0.1790	0.0001	0.0001	0.0001

NS = not significant p-value > 0.25

different elements draws into question the assumption that soil ingestion is a log-normal process. Clearly, adding constants to soil ingestion estimates prior to taking the logarithm exasperated the lack of normality.

Another area of controversy in analysis of soil ingestion data is the handling of exceptionally large or unusual values. A general data analysis principle designed to maintain the integrity of the study requires that all soil ingestion estimates should be retained in an analysis unless there is substantial reason to doubt their validity. In the UMass study, both exceptionally large values, and unusual values occurred.

There were four instances where soil ingestion estimates were unusual for a subject for a given element. Identification of these unusual estimates was based on a comparison of the estimates with other estimates for the element for the sample of subjects using methods for identifying outliers. Although four measures were so identified as outliers, whether they were simply unusual values, or invalid values is an issue. Since soil ingestion estimates were made for these subjects using seven other tracer elements, and in each case, there was no evidence of unusually large (or small) soil ingestion estimates, the unusual values in question were judged to be invalid. It is likely

Table 3 *Log (soil ingestion + 0.1 mg day^{-1}) estimates for the five lowest children and the five highest children (n = 64).*

Element	Lowest 1	2	3	4	5	Highest 60	61	62	63	64
Al	−3.7	−2.9	−2.9	−2.6	−2.5	−1.3	−1.1	−1.0	−0.8	1.9
Si	−3.1	−3.0	−2.7	−2.6	−2.6	−1.1	−1.0	−0.9	−0.4	1.7
Ti	−3.9	−3.6	−2.5	−2.5	−2.4	−0.1	0.4	0.7	1.5	1.9
V	−5.4	−2.3	−2.3	−2.3	−2.2	0.6	0.7	1.0	1.6	1.8
Y	−4.9	−4.1	−3.8	−3.3	−3.1	−1.6	−1.6	−1.5	−1.5	1.9
Zr	−3.6	−3.5	−3.4	−3.0	−2.7	−1.6	−1.6	−1.4	−1.4	0.4

that some measurement error was made in estimating the tracer for these subjects, although it was not possible to identify the source of the error.

One exceptionally large value was reported consistently for all tracers for a child who consumed on the order of 5–7 g day^{-1}, while estimate of median soil ingestion in the sample of 64 children was in the range of 0.01–0.1 g day^{-1}. Thus, this child had between one and two orders of magnitude higher soil ingestion. It is instructive to look at the five lowest and five highest log (soil ingestion) estimates, after adding 100mg to each to remove some negative values. The results are given in Table 3 for several elements.

For all elements except Ti and V, the 64th subject (the pica subject) appears as an outlier on the distribution of soil ingestion. Since this individual is so different from all the others observed in the study, any parametric analysis of soil ingestion data will be sensitive to this value. For this reason, many summaries of soil ingestion have this subject excluded. Nevertheless, since the behaviour of this subject is of special interest, complete details on soil ingestion results are presented separately (Calabrese *et al.*, 1991). We feel that the approach of identifying and describing true outlier values in detail, but summarizing the major sample data separately permits clearer understanding of soil ingestion.

Conclusions

Although much of the discussion in this paper has dwelt on the inappropriateness of many techniques for analysis of soil ingestion data, there are methodological approaches that are sound and feasible. The basic approach we recommend is non-parametric, where inference is not based on some assumed theoretical sampling distribution, but is based rather on arguments for inference built directly from selecting a sample. The median and percentiles as population characteristics are emphasized, for reasons summarized elsewhere (Stanek *et al.*, 1990). Test statistics and *p*-values can be motivated directly from sampling based arguments, and require making the assumption simply that subjects in each group were selected via simple random sampling. The strengths of the analysis approach are self evident, since limited assumptions are required. The analysis approach will not be sensitive to outliers or extreme values, since rank transformations have been used. When such methods are used, the resulting summary will be clearer and more robust.

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Determination of Human Exposure to Lead and Cadmium: A WHO/UNEP Pilot Study

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Abstract

In Stockholm, methods for measuring exposure to lead and cadmium from air, food and beverages were studied in 1988 in a group of 15 non-smoking women, as part of the WHO/UNEP HEAL programme. Airborne particles in the breathing zone air (24-hour samples), duplicate diets (24-hour samples), and faeces (all the stools produced) were collected during 7 consecutive days. Blood was sampled before and immediately after the study period. The results confirmed the need for personal monitoring in the assessment of human exposure to lead and cadmium via air and food. There is need for suitable equipment for 24-hour personal air monitoring. On average, dietary lead (26 μg day^{-1}, SD 7.9) contributed more than 80% of the total lead uptake, while dietary cadmium (8.5 μg day^{-1}, SD 2.1) contributed about 99% of the total cadmium uptake. Occasionally consumed foodstuffs with high levels of lead or cadmium seemed to be responsible for a large part of the total weekly intake of lead and cadmium. Faecal lead and cadmium were found to be useful indicators of the total amounts of these metals ingested. Due to the large day-to-day variation observed in the dietary intake of lead and cadmium, the sampling period for duplicate diets and faeces should be at least 5–6 days.

Introduction

The World Health Organization (WHO) and the United Nations Environment Programme (UNEP) are coordinating an international exposure assessment effort – the Human Exposure Assessment Locations (HEAL) programme (UNEP/WHO, 1985, 1986). In one of the first projects methods for monitoring exposure to lead and cadmium from air, food and beverages were studied during one week in small groups of non-smoking women, 23–53 years of age, in Beijing, Stockholm, Toronto and Zagreb. The main objective was to develop the best methods for monitoring personal exposure to lead and cadmium, including methods for quality assurance. A report of the international studies has recently been published (Vahter and Slorach, 1990). The present report briefly describes the methods used in the determination of human exposure to lead and cadmium. The evaluation is based mainly on the exposure study carried out in Sweden (Vahter *et al.*, 1991).

Materials and Methods

Samples of airborne particles, duplicate diets, faeces and blood were collected in a group of 15 non-smoking women, 27–46 years of age, in Stockholm in February–March 1988. Questionnaires concerning personal data were completed by each woman. All containers and other equipment used for sampling, storage and sample preparation were checked to ensure that they did not release lead or cadmium.

Total suspended particles in the breathing zone of each subject were sampled during 7 consecutive 24-hour periods using low-volume personal air samplers (Casella T 13350), with a flow rate of 2 L min^{-1}, and 37 mm membrane filters with 0.45 μm pore size.

To determine ingested lead and cadmium, duplicates of all foods and beverages, including drinking water, but not certain medicines or chewing gum, were collected as 24-hour samples during the 7 consecutive days. Daily food records were completed by each participant. The subjects did not have to weigh each food item consumed, since it was feared that the extra work and inconvenience this involved would influence their food intake. Consumption of canned food, which may contain much more lead than the corresponding fresh foods (Slorach and Jorhem, 1982), and the approximate volume of beverages were recorded. The women had daily meetings with the study supervisor. Any change in food consumption habits due to sampling procedures or any foods ingested, but not duplicated, were noted in a food record follow-up questionnaire on a day-to-day basis.

All faeces corresponding to the food and beverages ingested during the 7 days were collected. In order to indicate the faeces to be collected, a colored marker (carmine red) was ingested at the beginning and at the end of the duplicate diet collection period. The first colored stool, representing the first duplicate diet collected, was collected. The second colored stool, representing food and beverages ingested after the duplicate diet collection period, was not included.

Blood (10 mL venous blood) was collected at the beginning of and immediately after the study period of 7 days, for evaluation of the total exposure to lead and cadmium.

Quality control (QC) samples (both internal QC samples

† *Special issue incorporating the Proceedings of the Symposium on the Bioavailability and Dietary Exposure of Lead*

with concentrations of lead and cadmium known to the analyst, and external QC samples with concentrations not known to the analyst) of all the media involved were analyzed together with the monitoring samples. The preparation of the QC samples (spiked bovine blood, freeze-dried human faeces, spiked membrane filters, house dust, and freeze-dried simulated human diets) has been described by Lind *et al.* (1988), and Jorhem and Slorach (1988). The analytical performance evaluation involved the analysis of sets of 6–12 QC samples and evaluation of the analytical results using linear regression analysis (Vahter and Friberg, 1988). For acceptance, the regression line of the reported versus the reference values had to fall inside a given interval. The ranges of concentrations of lead and cadmium in the QC samples were chosen to cover the ranges of concentrations expected to be found in the monitoring samples collected in the various participating countries. The analytical procedures have been described elsewhere (Vahter and Slorach, 1990).

Results and Discussion

The results of the quality control analyses carried out together with the analyses of the monitoring samples were in good agreement with the reference values. However, some of the monitoring samples contained less lead and cadmium than expected and the lowest concentrations were not always covered by the range of QC samples (Vahter *et al.*, 1991).

The concentrations of lead in blood of the 15 women ranged from 15 to 44 μg Pb L^{-1} (median 28, mean 29, SD 8.3). The concentrations of cadmium in blood ranged from 0.1 to 0.8 μg Cd L^{-1} (median 0.3, mean 0.3, SD 0.16).

The main sampling problems were associated with the personal 24-hour monitoring of airborne lead and cadmium. Since the commercially available personal air monitors are designed for occupational exposure monitoring of 8-hour periods it was necessary to recharge the batteries every 6–8 hour. When the subject was not moving, the pump was connected to the mains. Furthermore, the pumps were noisy. It was concluded that there is a need to develop better equipment for 24-hour personal air sampling.

The concentrations of lead and cadmium in breathing zone air were very low during the study week, probably partly because the women spent about 90% of their time indoors. The weekly average concentrations of lead in breathing zone air ranged from 42 to 94 ng m^{-3} (mean 64, SD 14). The concentrations of cadmium ranged from 0.5 to 1.1 ng m^{-3} (mean 0.8, SD 0.16). On average, airborne cadmium contributed about 1% to the total uptake of cadmium, while airborne lead contributed about 15% to the total uptake of lead. In a full-scale study, on a representative sample of the general population in Stockholm, it would not be essential to carry out personal air monitoring of cadmium. Personal monitoring of exposure to airborne lead might be useful in areas with heavy traffic during seasons when people spend more time outdoors.

A total of 105 daily duplicate diets were collected. The content of lead and cadmium ranged from 4.4 to 130 μg Pb per diet and 1.8 to 56 μg Cd per diet. The average daily dietary intake of lead during the 7 day period for the 15 subjects was 26 μg (SD 7.9, range 13–40). The corresponding cadmium intake was 8.5 μg (SD 2.1, range 5.7–14). On average, dietary lead contributed more than 80% of the total lead uptake, while

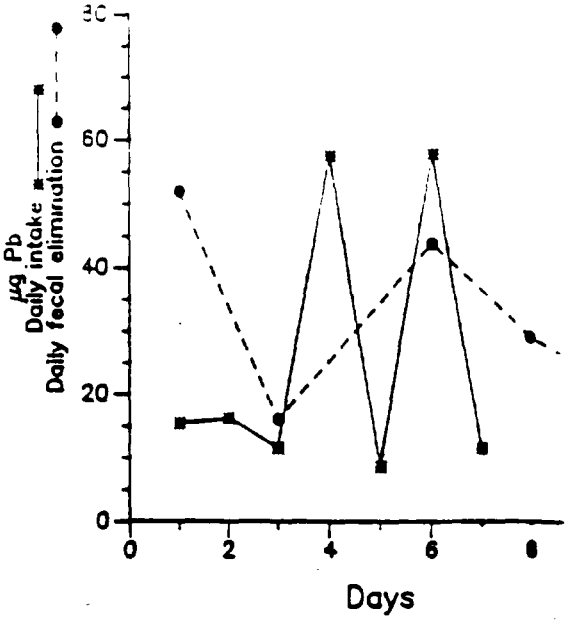

Figure 1 *Example of day-to-day variations in [illegible] and faecal elimination of lead by one subject [illegible] week.*

dietary cadmium contributed about 99% of [illegible] uptake.

There were large day-to-day variations [illegible] intakes of lead and cadmium. One daily diet [illegible] more than 50% of the total weekly intake of [illegible] This indicates that certain occasionally consumed [illegible] responsible for a large part of the total dietary [illegible] metals. Evaluation of the food records made [illegible] associate some of the observed high levels of [illegible] in the 24-hour duplicate diets with certain foods, [illegible] lead in canned food and wine, and cadmium in [illegible] *et al.*, 1990).

The large day-to-day variations in the dietary [illegible] lead and cadmium has to be considered when [illegible] method for measuring dietary intake. The duplicate diet [illegible] is probably more suitable for measuring dietary [illegible] and cadmium than methods based on the analysis of [illegible] foods combined with food consumption data. However, it should be noted that the food intake may decrease, and the food consumption pattern may change due to the duplicate sampling. In the Swedish study group there was no indication of markedly decreased food intake due to the duplicate sampling. The daily intakes of foods and beverages (307–477 g dry weight) did not indicate a low food intake. According to the food record follow-up questionnaire the women had collected essentially everything ingested, and only minor changes in dietary habits were noted, for instance eating half an apple instead of a whole one because the subject had one apple and half of it had to be put in the duplicate container.

The large day-to-day variations in dietary intake have to be considered also when deciding on the number of days and persons to be studied. In order to evaluate the number of days required for reliable estimates of dietary intake, average daily intakes of lead and cadmium were calculated for 2, 3, 4, 5 and 6 days of sampling for each person, and the

to the 7-day average. With 3 days of sampling the average daily intake of lead and cadmium was about 90% of the 7-day average, indicating a reasonably good estimate on a group basis. However, the variation between individuals was large (range 28–149% for lead, and 48–112% for cadmium). With 6 days of sampling the variation decreased for both lead (range 84–115%), and cadmium (range 89–112%). Thus, it was concluded that six days were required to obtain reasonably good estimates on an individual level (Vahter *et al.*, 1991). Longer periods of duplicate diet collection may influence the food consumption pattern.

All the women in the Swedish study group reported complete faeces collection. The faecal elimination of lead and cadmium was calculated from the total amounts of lead and cadmium eliminated during the sampling period, and compared with the metal contents of the duplicate diets collected during the 7 days. The total faecal elimination, expressed as a percentage of the dietary intake, was 104% (range 72–158%) for lead and 113% (range 74–148%) for cadmium. It can be estimated that only a minor part (about 5%) of the lead and cadmium in faeces originated from the faecal excretion of endogenous lead and cadmium (Chamberlain, 1985; Elinder, 1985; Nordberg *et al.*, 1985). A reason for high recoveries may be that the faeces collected did not correspond exactly to the food collected. Some of the first colored faeces samples collected contained 2–9 times as much lead or cadmium as the corresponding duplicate diet (Figure 1). Since the duplicate diet collection started at 3 pm, at which time also the colored marker was ingested, a high dietary lead or cadmium intake earlier that day or the day before may have influenced the first colored faeces samples.

When the first colored faeces samples with metal contents exceeding the corresponding first duplicate diet by 2–9 times were excluded, the average faecal elimination of lead, adjusted for excretion of endogenous lead, was 85% (range 59–121%) of the dietary content, which is consistent with the reported 10–20% average gastrointestinal absorption of lead in adults (Chamberlain, 1985; Rosen, 1985; Tsuchiya, 1986). The corresponding figure for cadmium was 97% (range 66–144%), which is consistent with the 5% average gastrointestinal absorption of cadmium (Friberg *et al.*, 1986). However, even after the adjustments the faecal elimination of lead and cadmium in some women exceeded the amounts found in the duplicate diets, indicating incomplete duplicate diet collection or other sources of lead and cadmium besides the diet. It could be estimated from the air filter samples that the contribution to faecal lead and cadmium from particles inhaled, cleared from the lungs and swallowed, was negligible (Vahter *et al.*, 1991). Other sources of peroral lead, such as toothpaste, lipstick *etc.* were not investigated in the Swedish study.

Faecal lead and cadmium may be used as indicators of the total amounts of these metals ingested. Feces collection does not influence the food intake or the food consumption pattern. It is considerably cheaper than the duplicate diet technique and in many cases less inconvenient for the subjects involved. The first colored stools appeared between days 1 and 5, indicating large variations in the gastrointestinal transit time. The average daily faecal elimination of lead (24 μg, SD 9.7, range among subjects 10–41 μg) and cadmium (8.9 μg, SD 2.0, range among subjects 5.5–12 μg) was calculated by dividing the total faecal metal content during days 3 to 8 of the test period (for one subject days 5 to 10) by 6. In order to evaluate the number of study days required for reliable estimates of faecal elimination, the average daily faecal elimination calculated for 2, 3, 4 and 5 days for each person were related to the 6-day average. The interindividual variations decreased with the number of days studied for both lead and cadmium. With 4 days of sampling a reasonably good estimate on a group basis was achieved. The average faecal elimination of lead was about 90% of the 6-day average, but the range was still wide (23–130%). With 5 days of sampling the faecal lead elimination in percent of the 6-day mean ranged from 71 to 115%. The data for cadmium were similar. Thus, it was concluded that at least five days were required to obtain reasonably good estimates on an individual level (Vahter *et al.*, 1991).

Conclusions

The results confirm the need for personal monitoring in the assessment of human exposure to lead and cadmium via air and food. There is a need to develop better equipment for personal air sampling.

The duplicate diet collection period should be 5 days in order to obtain reasonably good estimates of dietary intake of lead and cadmium. The diet was the major source of exposure to both lead and cadmium. Locally consumed foods seemed to be responsible for a large part of the total intake of lead and cadmium.

On a group basis, faecal lead and cadmium [illegible] for validation of the duplicate diet collection efficiency. Lead and cadmium were found to be useful indicators of the amounts of these metals ingested. Due to the large individual variations in dietary intake of lead and cadmium, and differences in the gastrointestinal transit time, the faeces sampling period should be at least 5 days.

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Methods for Assessment of Dietary Lead Exposure of the Inner-City Population

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Abstract

Assessment of dietary lead exposure of individuals begins with the determination of food and beverage intake by the individuals, and concludes with an evaluation of the lead content of the foods and beverages consumed. Of several techniques available for assessment of dietary intake, the 24–hour food recall is recommended as the method of choice for assessing current dietary lead intakes in inner-city populations. The three–day food record can be used among cooperative and motivated subjects, while the dietary history method is available for assessing long-term intakes in the past. The unavailability of lead content values of a large number of foods will to a large extent restrict the use of these methods in large-scale dietary lead exposure studies. Until the time that such data becomes available, the most accurate estimates of lead intake can be provided by chemical analysis of duplicate samples of foods consumed, as is currently done. However, this method is feasible only for small samples.

Introduction

Assessment of dietary lead exposure of populations begins with the determination of food and beverage intake, followed by an evaluation of the lead content of the foods and beverages consumed. This paper represents a detailed description of methods used for dietary assessment of human populations. It begins with an overview of the dietary assessment process, followed by a description of the dietary assessment techniques and a discussion of their advantages and disadvantages with particular reference to their application in minority populations. It concludes with a description of additional data needs for assessment of dietary lead exposure.

Overview of Dietary Assessment

Dietary assessment is one of four procedures used for evaluation of the nutritional status of individuals. It can be defined simply as the determination of the intake or the adequacy of intake of foods, food energy, nutrients or other dietary constituents. The dietary assessment procedure involves the collection of qualitative or quantitative data on foods and beverages consumed during a certain time period.

If qualitative data are collected, the data can be examined to determine if the diet is balanced (*i.e.* if all of the four food groups – the meat group, the milk group, the fruit and vegetable group, and the grain group – are represented among the foods and beverages consumed). If quantitative data are collected, the intakes of food energy, nutrients or other dietary constituents can be calculated. The average daily intake of food energy and nutrients can then be evaluated by comparison with the US Recommended Daily Allowances (RDA) or with the Estimated Safe and Adequate Intakes for those nutrients for which there are no RDA (National Research Council, 1986). Alternatively, the number of servings of foods consumed from each of the four food groups can be calculated and compared with the recommended number of servings of foods that should be consumed from each of the four food groups. For example, the numbers of servings that should be consumed by adults from the meat, milk, fruit and vegetable, and grain groups are 2, 2, 4 and 4, respectively.

Another method of evaluation of quantitative dietary data is the calculation of the dietary score (Guthrie and Scheer, 1981). The dietary score is an overall index of the quality of a diet based on the four food groups.

Dietary Assessment Techniques

Four methods are used for dietary assessment of individuals. These methods can be classified as either retrospecuve or prospecuve (Pao, 1989).

Retrospective methods include: (1) the recall of past actual food intake, *e.g.* the 24–hour food recall; and (2) the recall of past usual intake, *i.e.* the dietary history.

Prospective methods include: (1) the food record or diet diary of actual food intake; and (2) the weighed food intake.

Recall of past actual food intake

In the recall of past actual food intake the subject, or caregiver if the subject is a child, is asked to recall the kinds and amounts of all foods and beverages consumed during some time period in the immediate past. The most frequent time period used is 24 hours, in which case the method is called the "24–hour Food Recall".

Detailed descriptions of the foods and beverages consumed (including brand names) and their preparation methods are recorded (National Research Council, 1986). Portion sizes may be estimated in household measures (cup (8 fluid ounces), teaspoon or tablespoon); counts for those food items that can be counted (*e.g.* slices of bread, eggs or fruit) or dimensions for those items that cannot be measured by either of the methods described above (*e.g.* meat, cake or pie).

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An important advantage of this method is that it can be conducted within a relatively short time – 15 to 30 minutes, so that it can be conducted in one interview. Therefore, the method is relatively inexpensive. Dietary practices are not usually affected, and the respondent burden is light so that the response rate is usually high. Also, it can be used with illiterate or semi-literate subjects. A major disadvantage is that accuracy is dependent on the respondent's memory. This can be a major problem. Further, one day's food intake may not be representative of usual intake.* A source of error is poor estimates of portion sizes if quantitative data are being collected.

Dietary history

In the dietary history method, the respondent is asked by a trained interviewer to recall the usual food intake during some time in the near or distant past. It may include recall of a typical day's food and beverage intake during the specified time period and/or a food frequency. The typical day food recall is similar to the 24–hour food recall except that the focus is on food and beverage consumption during the 'typical' day selected by the respondent. The respondent is exhorted not to select holidays or 'celebration' days as typical days.

The food frequency consists of food and beverage items or food groups, usually representing the more commonly consumed foods and beverages. Respondents are asked to indicate which items were consumed and, if consumed, the frequency of consumption of the item during the specified time period. Frequencies may be given in terms of number of days, number of times or in terms of such measures as daily, weekly, monthly, yearly or never. Quantified food frequencies provide information on the frequency of consumption of regular portion sizes of the food and beverage items. Food frequencies may also be used in combination with the 24–hour recall or with the food record and weighed food intake methods. In this case, the time period for the food frequency may be the past week. Food frequencies are a favorite dietary assessment tool of epidemiologists, as it quickly gives a picture of overall food intake (Pao, 1989).

The dietary history method was originally developed for use in studies of the relationships between diet and physical growth, clinical and biochemical measures of nutritional status, and disease states, all of which may be more reflective of long-term dietary intake (Pao, 1989). Therefore, a major advantage of the method is that it can be used to assess long-term dietary intakes. The method can also be used to provide information on food habits, changes in food habits over time, food preferences and seasonal variations in food intake.

However, there are several disadvantages. Respondent burden is high because of the need to recall characteristics of diets consumed some time ago. Because of this, highly trained and skilled interviewers are needed, thereby increasing the costs of data collection. The method can be time-consuming, a fact which further increases the costs of data collection. Also, the method has been found to lead to [illegible] intakes (Burk and Pao, 1976).

Food record/diet diary

In the food record or diet diary method, the respondent is to record, at the time of consumption, the nature and qua of all foods and beverages consumed during a specifie period (Gibson, 1990). The time period most frequently three days, in which case the method is called the "Thr Food Record". The three days usually include two wee and one weekend day collected consecutively. Similar on the foods and beverages consumed as have been des for the 24–hour food recall method are recorded.

The food record is generally considered to be accurate than recall methods as it does not rely on me Indeed, the accuracy can be high in those instances whe respondent is quite conscientious in maintaining the r Another advantage of the method is that it is representative of the usual diet since it covers a longe period than one day.

One disadvantage of the method is that it requires bit of cooperation from the respondent because of the t of maintaining the record. Because of this response rate to be low, especially in subjects of low socio-ec Subjects must be literate, a fact which can further participation of illiterate or semi-literate persons, are not used to maintaining records. Poor estimates of p sizes or omissions of food items are considerable and co sources of error. In the case of omissions, this can be cor by having the interviewer review the daily record of respondent. Any items omitted can then be added to However, this will add to the cost of data collection. training of the respondent in how to maintain proper records is required. The more trained the respondent is, the accurate and clearer the record will be.

The method tends to cause some changes in consumption practices. Either the subject may consume a diet in order to impress the interviewer or the diet is simplified so as to make record keeping easier. Small amounts of foods consumed away from home may n estimated as accurately as food consumed at home

Weighed food intake

In the weighed food intake method all foods to be consum the individual are weighed and the weight recorded, usu grams. After the meal or snack, any plate waste is weighe the weight of food consumed can then be obtain difference. Instead of weighing, the volume of liquids measured. Weighed food intake data are usually collect one to seven days, depending on the resources ava Detailed descriptions of the foods and beverages consum recorded as has been described previously.

One important advantage of this method is tha potentially the most accurate method for collecting dietar However, a major disadvantage is that it the most diffi all the methods. If the interviewer has to do the weighin there is a great burden on the interviewer. This would se limit the number of subjects that can be studied at one tim burden can be shifted from the interviewer by trainu subjects to conduct the weighing and recording. In this ca method becomes a weighed food record with the

* In order to estimate usual intakes of individuals, repeated 24–hour food recalls are conducted. The US Committee on Food Consumption Patterns has recommended that four 24–hour food recalls be conducted on the same individual over as one-year period in order to estimate his/her usual food intake (National Research Council, 1986). For assessing average intakes of groups, a single 24–hour food recall of each individual in the group is sufficient.

disadvantages previously described for the food record method. Additional disadvantages of the weighed food intake are that it is time consuming and expensive, especially where respondents must be provided with scales and other measuring implements.

Collection of 24–hour Food Recall Data

In our own work on assessment of current dietary intakes of inner-city populations, we have mainly used the 24–hour food recall method. In fact, the 24–hour food recall is the most commonly used dietary assessment method in large-scale studies of most populations. Therefore, detailed information is presented on the collection of 24–hour food recall data.

The collection of quantitative 24–hour food recall data requires some attention to detail. The amounts of foods and beverages consumed are collected in terms of common household measures (cup, teaspoon, tablespoon) or regular portion sizes. In order to do this properly, certain visual aids must be used during the interview. Examples of such visual aids are:

(1) A teaspoon and a tablespoon.
(2) A serving spoon.
(3) A set of measuring spoons.
(4) A measuring cup set.
(5) Representative cups and glasses of various sizes – each graduated in fluid ounces; or portions of a cup; or number of cups.
(6) Representative bowls of various sizes each graduated in cups.
(7) A ruler to measure portion sizes that cannot be quantified in terms of cups, teaspoons or tablespoons.
(8) Plastic models (or, less preferred, life size pictures) of regular portion sizes of the more commonly consumed foods.
(9) Lunch and dinner plates on which to arrange the food models.

Good sources of food models are Nasco (Fort Atkinson, Wisconsin) and Iwasaki Images (Modesto, California). These visual aids are used by asking the respondent to estimate the quantity of food or beverage consumed in relation to the amount represented by the visual aid. Studies have shown that the accuracy of quantitative dietary data collected is improved when such visual aids are used (Moore *et al.*, 1967). Needless to say, visual aids are not needed if qualitative dietary data are being collected.

Additional Data Needs for Assessment of Dietary Lead Exposure

The dietary assessment techniques described above were designed for evaluation of the intake of food energy, nutrients and other dietary constituents and not for lead, this not being considered an essential nutrient. Although the same techniques can be used for assessment of dietary lead exposure, some additional data are necessary. Such additional data which would need to be collected include the use of food processed in lead-soldered cans or packaged in containers imprinted with lead-containing paint; the use of ceramics decorated with lead-based paints; the use of lead crystal (though this is probably an insignificant source of dietary lead exposure in most populations); the use of cooking utensils repaired with lead solder; and the practice of pica, particularly with regard to the consumption of lead-based paint chips.

Another important data need, particularly for the calculation of lead intake, is information on the lead content of a large number of foods. At the present conference, it was reported that the Food and Drug Administration has data on the lead content of 232 foods. In the short term, such data can be used for calculation of lead intake if the appropriate substitutions are made. For example, if the lead content of apple pie is available, then the same value can be used for all fruit-filled pies such as cherry, peach, *etc.* However, there is a limit to which such substitutions can be made, *e.g.* it may be difficult to justify using the lead content of apple pie for other types of pies such as lemon meringue, custard, or sweet potato. Therefore, until the data base for lead content is extended to include a wider range of foods, any calculations of lead intake based on any of the dietary assessment techniques described herein, should be regarded as providing only rough estimates. More accurate estimates of lead intake can be provided by chemical analysis of duplicate samples of foods consumed. However, such a method is limited to small samples and is not feasible for large-scale field studies.

Conclusions

In conclusion, the 24–hour food recall is recommended as the method of choice in assessing current dietary lead exposure in inner-city populations. For a cooperative and motivated sample, the three–day food record can be used. The dietary history is the only method available for assessing long-term intakes in the past. While each of these methods has its limitations, if properly used and interpreted, and if supplemented with the appropriate data, each is capable of giving a fair estimate of dietary lead intake. One major deterrent to the use of these methods in large-scale dietary lead exposure studies is the unavailability of lead content values of a large number of foods. At the present time, the most accurate estimates of lead intake are provided by chemical analysis of duplicate samples of foods consumed, a method feasible only for small samples.

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The Drive to Lower Lead Levels in Food Chemicals*

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Abstract

Because chemicals that are intentionally added to food during its production constitute a significant portion of the US diet, reducing lead levels in them is one of the long-term objectives of the Committee on Food Chemicals Codex, a committee of the Food and Nutrition Board within the Institute of Medicine. The Committee recommends limits for lead, as well as for other heavy metals, arsenic, and other potentially hazardous constituents in chemicals used in food production. The Food Chemicals Codex is a compendium of purity specifications that often become legal standards for food chemical purity in the United States and in many countries worldwide. The Committee plans to lower existing lead limits for food chemicals based on their level of consumption or reported use. Data regarding food chemical use is available from the 1987 Poundage and Technical Effects Update of Substances Added to Food. *Because of their high level of consumption, sweeteners constitute a group of food chemicals in which lead limits could be lowered. However, the Committee's ability to recommend lower lead limits in these products depends on the availability of a test method capable of measuring lead at lower levels. This Committee intends to make its contribution in the effort to lower dietary intake of lead.*

Introduction

For decades, there has been heightened concern regarding lead exposure from all sources in the environment, including the diet. This concern is exemplified by recent findings showing that deleterious neurobehavioural effects are observed in children exposed to minute amounts of lead (Needleman, 1990). It is therefore critical that lead exposure from all sources be reduced as much as possible. During the 1980s, a general decline in overall lead exposure was attributed largely to the discontinued use of lead solder for packaging canned foods and in gasoline production. Now that lead exposure from these sources is declining, attention is turning to other sources, such as dietary intake, for which lead exposure can be further diminished.

Food chemicals represent one dietary source in which reductions in lead intake may be attained. This premise is especially justified for those food chemicals consumed in large amounts, perhaps constituting up to 2!3 percent of the diet in significant proportions of eaters. Of course, lead is not intentionally added to food, but it is inadvertently introduced as an environmental contaminant during food processing and is also known to be present in some source food materials (*e.g.*, crop plants). As overall levels of dietary lead intake decline, food chemicals may represent an emerging source of lead. Therefore, in concert with the drive to lower overall lead exposure, lead in food chemicals should be limited to their lowest level possible.

* The term food chemicals used in this paper represents any substance used in the production of food, including substances that are generally recognized as safe (GRAS), food and color additives, and processing aids, but excluding pesticides and indirect food additives.

The Food Chemicals Codex

Food Chemicals Codex specifications often become legal standards for food chemical purity in many countries worldwide. In the United States, the Food and Drug Administration (FDA) may adopt a monograph containing specifications as its legal basis for determining food-grade purity for the food chemical specified in that monograph. In Canada, Australia, and many other countries, *Food Chemicals Codex* specifications are adopted automatically as stipulated in their respective food laws. To harmonize purity specifications worldwide and to facilitate the international trade of food chemicals, the *Food Chemicals Codex* conveys its proposed specifications to a number of other international organizations such as the United Nations' Codex Alimentarius Commission.

The Committee on Food Chemicals Codex started in 1961 in response to a need expressed by the FDA, the public, and the food industry. Almost 30 years later, the Committee plans to publish a third supplement to the third edition to the *Food Chemicals Codex* in 1991, and a fourth edition in late 1993 or early 1994.

The purpose of the *Food Chemicals Codex* is to specify food-grade quality for food chemicals (NRC, 1981). Specifications for these substances are published in monographs that contain assay specifications to identify the major constituent, as well as purity specifications for secondary constituents and contaminants such as lead. Each specification includes a recommended limit and a test method that enables food chemical manufacturers and customers to comply with the limits.

One of the Committee on Food Chemicals Codex's long-range objectives is to develop a policy to recommend lower lead limits for food chemicals as part of their goal to

Table 1 *Food chemicals selected from the 1987 Food Additives Survey*

Food chemical	1987 Poundage value
Fructose	3,031,040,886
Sucrose	2,732,418,809
Corn syrup	1,976,761,536
Soybean oil	1,286,550,001
Soybean oil, hydrogenated	1,077,217,163
Sodium chloride	681,719,817
Sucrose, liquid	604,096,584
Carbon dioxide	380,755,664
Corn oil	336,590,016
Dextrose	175,438,897
Whey	151,032,200
Calcium carbonate	124,203,460
Coconut oil	97,750,003
Caramel color	93,949,653
Diatomaceous earth	86,705,058
Food starch, modified	86,156,938
Cottonseed oil	86,050,349
Starch, modified	85,199,263
Sodium hydroxide	75,597,597
Citric acid	64,179,529
D-sorbitol	63,861,826
Corn syrup solids	61,853,969
Lactose	53,801,539
Calcium oxide	47,247,476
Cottonseed oil, partially hydrogenated	47,099,238

reduce dietary lead intake. This objective is being driven by the Committee's recognition of recent evidence that deleterious neurobehavioural effects in children occur at levels below those previously considered acceptable. When feasible, the Committee intends to lower the lead limit as much as possible, and will first examine those food chemicals consumed in large quantities, especially in children. However, two limitations restrict the Committee's ability to recommend lower lead levels: the feasibility of the existing analytical methodology and the paucity of intake data.

Analytical Methodology

Ostensibly, it would appear to be a simple task for the Committee to earmark high-volume food chemicals and then recommend a lower lead limit for them. However, the Committee has a major hurdle to overcome: the existing colorimetric test method for lead determination specified in the *Food Chemicals Codex* is outdated and not sensitive enough to accurately measure lead at the lower levels of interest. Except for edible oils, a suitable method of analysis is not yet available. The Committee has accomplished some work towards lowering lead limits, however. A graphite furnace-based atomic adsorption spectrophotometric test method for edible oils (*e.g.*, coconut oil) with a specified lead limit of 0.1 mg kg^{-1} (100 ppb) was published in the second supplement to the *Food Chemicals Codex* (NRC, 1986). This method may be applicable to other high-volume food chemicals with some adaption.

Previous limits of analytical sensitivity are being ove as new research methods become available; they are be published continually. However, these methods are often suitable for the purposes of the *Food Chemicals Codex* suitable analytical method, specifically intended for purposes of monitoring and compliance, must be based on following criteria: adequate sensitivity, selectivity, accur precision, simplicity, and low cost. Moreover, it must be ba on instrumentation with wide-range applicability accessibility to many types of analysts, either in-house or suitable contract laboratory. Most available research meth do not satisfy all of these criteria. Eventually, a suitable me will be developed by adapting a widely-used well-established collaborative research method.

Sources of Intake Data

It is difficult at this time to estimate accurately the level of intake from food chemicals relative to that from the total because of the lack of intake data. Food chemicals are usually consumed as is, but are typically consume components of processed foods. In addition, the rel contribution of dietary lead from food chemicals to that food packaging components (such as lead-soldered cans) i known, or with best estimates, is fraught with uncertainty

One source of food chemical use information availat the Committee is the *1987 Poundage and Technical E Update of Substances Added to Food* (1987 Food Addi Survey). Initially, the Committee intends to use the 1987 Additives Survey data to identify particular food chemica categories of food chemicals, to consider for recomme lower lead limits.

Based on the 1987 Food Additives Survey sweeteners appear to be a reasonable category of chemicals for which lead limits could be lowered, justifi their high level of use (see Table 1). In addition to sweete the Committee intends to establish similarly lo recommended lead limits for other high-volume chemicals.

Another potential source of intake data is the F ongoing Total Diet Study (TDS) (Pennington, 1983). Spe products in prescribed food categories are randomly taken store shelves, aggregated, and then analyzed for both nut and environmental contaminants such as lead. The foods chosen for analysis are based on data from the Nationwide Consumption Survey (conducted by the US Departme Agriculture) and the Second National Health and Nut Examination (carried out by the National Center of H Statistics). The TDS provides lead levels in small numb food samples with a high degree of accuracy. However, this approach to estimate lead intake in many individual items consumed can be prohibitively expensive to perfor

A variant of the TDS approach, the Dietary Exp Assessment Method or DEAM, has recently been pub (Graham *et al.*, 1990). In the DEAM approach, 10 to 2(products, each with a known market share, can be aggr into a composite sample that can be analyzed for a vari contaminants such as lead. In detail, the number of products combined in a composite sample is limited l sensitivity of the analytical method because the analyte n

diluted as more products are added to the composite sample. The food categories selected for the composite sample could be based on their weight percent of the total diet (Pennington, 1983). Once the categories have been selected, specific foods, based on their market share, could be incorporated in the composite sample. Therefore, a composite sample containing the top market share food products representing the top 20 food categories could yield a quantifiable estimate of lead intake to the general public. If intake data become available produced by the TDS or DEAM, the Committee may consider those data to help their efforts to recommend lower lead limits.

Conclusion

The Committee on Food Chemicals Codex of the Institute of Medicine intends to contribute to the effort to lower dietary intake of lead. Whenever possible, the Committee intends to recommend lower lead limits in food chemicals with high levels of use. The feasibility of the existing analytical methodology and the paucity of intake data restrict the Committee's ability to recommend lower lead levels. In the future, newer, more suitable analytical methods plus intake data should become available for the Committee. Taken together, these activities of the Institute of Medicine can play a role in the drive to reduce dietary lead exposure.

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Lead Crystal: An Important Potential Source of Lead Exposure

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Abstract

We have examined the potential of alcoholic beverages to elute Pb from crystal wine decanters and glasses. Port containing 89 Pb L^{-1} was aliquoted into three lead crystal wine decanters. The wine Pb content rose steadily to a mean of 3,518 μg L^{-1} after 4 months. We then analyzed wines and liquors which had been stored in crystal decanters in the homes of our colleagues for periods of six months or longer. In the first four homes, eight decanters contained beverages with a mean Pb concentration of 7,781 μg L^{-1}. In a short-term experiment, white wine was found to elute small quantities of Pb from lead crystal glasses within minutes; the mean wine Pb concentration rose from 33 μg L^{-1} at time zero to a mean of 99 μg L^{-1} after four hours. We conclude that, in particular, lead crystal wine decanters are potentially an important source of Pb exposure for a segment of the population. In addition, lead crystal baby bottles, although not as widely available, were found to elute Pb into apple juice and infant formula; their sale should be banned.

Introduction

Historically, lead (Pb) has accidentally found its way into wines due to the use of leaden kettles, distillation devices, basins for mulling wine, leaden glazed pottery or lead cups (Nriagu, 1985). Ancient wines, to which Pb was intentionally added as a sweetener, have been estimated to have extraordinarily high Pb concentrations, approximately 20–30 mg Pb L^{-1} (Nriagu, 1985; Elias, 1985). Although the Greeks and Romans knew many of the 'classical' signs of Pb ingestion, including abdominal pain, constipation, pallor and palsy (Nriagu, 1983), they apparently did little to prevent Pb exposure via wine consumption, leading some to suggest that Pb poisoning was probably endemic (Gilfillan, 1965).

Early samples of Egyptian glass, dating back to 1500–1400 BC, have been found to contain 1–10% Pb (Nriagu, 1983). Lead crystal, with considerably higher concentrations of Pb, was invented in England in 1675 by George Ravenscroft, who discovered that the addition of Pb compounds to molten quartz yielded a glass with unique properties: high density, durability and brilliance due to visible light refraction (*Encyclopedia Americana*, 1984). The production and use of lead crystal glass increased rapidly in Europe during the eighteenth century. By the early nineteenth century, severe occupational Pb intoxication was described in glass workers in Paris (Tanquerel des Planches, 1848). In the USA, the production of lead crystal did not develop until the late nineteenth century (*Encyclopedia Americana*, 1984).

High quality lead crystal vessels now contain approximately 24–32% lead oxide (PbO). We have examined the potential of lead crystal wine decanters and glasses to elute Pb into alcoholic beverages, particularly wines. We have also examined the elution of Pb from lead crystal baby bottles, apple juice and infant formula. Our findings suggest that lead crystal glass may be an important 'new' source of Pb exposure.

Methods

Lead analyses: This laboratory is highly experienced in trace metal analysis and is certified by the OSHA for blood Pb analysis. Wine, liquor, juice and formula samples were analyzed for Pb content by a graphite furnace atomic absorption method traditionally used to analyze Pb in blood (Fernandez and Hilligoss, 1982).

Crystal wine decanters: Three crystal wine decanters were used in the initial experiment. Two of these, one Irish and the other French, were stated by the manufacturers to be 32% PbO; the other, West German, was stated to be 24% PbO. After carefully cleaning the mouth of the bottle, a bottle of port wine was opened and duplicate 5 mL samples were obtained for Pb analysis. The remaining wine was divided between the three vessels, and 5 mL samples were removed for Pb analysis after 2, 7 31, 84 and 127 days.

Colleagues were then canvassed to determine if their homes contained crystal decanters filled with wines or spirits for prolonged periods of time. Five faculty members responded; among them they offered the contents of 11 crystal decanters for Pb analysis. Plastic pipettes were used to obtain 5 mL samples from each decanter for the measurement of Pb content.

Crystal wine glasses: In order to determine the early time course of Pb elution from lead crystal glasses, we conducted an experiment meant to simulate consumption at the dinner table. Four sets of four glasses each were utilized. A set of unleaded

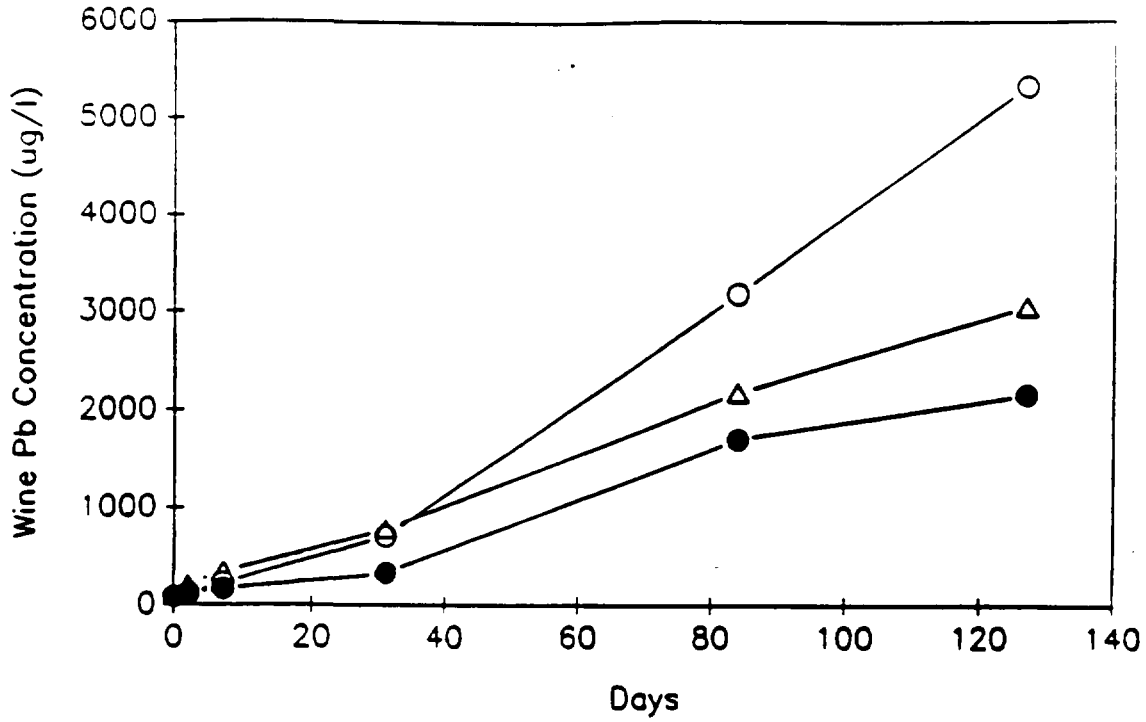

Figure 1 *Port wine Pb concentrations ($\mu g\ L^{-1}$) after storage in lead crystal wine decanters. A single bottle of wine apportioned into three decanters. The decanters were of French (open circles), Irish (open triangles) and German (closed circles) origin.*

crystal glasses served as controls. Two sets of lead crystal were of known PbO content; an Irish set (32% PbO) and a French set (24% PbO). A third set of Yugoslavian lead crystal glasses was of unknown PbO content. The geometries of the glasses varied considerably. The presence or absence of Pb in the glasses was confirmed by X-ray fluorescence using a Princeton Gamma-Tech XK-3 Lead-in Paint Analyzer (Princeton, NJ), kindly provided by the New York City Bureau of Lead Poisoning Control. All 16 glasses, as well as other glassware and pipette tips, were acid-washed with 0.5% HNO_3 (Ultrex) prior to the study.

At room temperature, two bottles of California wh were combined and mixed in a 2-L volumetric flask. D 5 mL samples were obtained for Pb and pH measur Using a 100 mL graduate cylinder (Pyrex), 80 mL also the wine were introduced into each glass. One mL sampl removed from each glass for Pb analysis after 10, 20, 60, 75, 90, 105, 120, 135, 150, 165, 180 and 240 m ANOVA was utilized to determine the effects of 'set' of and time in the glass on the wine Pb concentration.

Crystal baby bottles: We purchased two Irish lead cryst bottles (32% PbO) and two ordinary glass baby bottles. A

Table 1 *Pb concentrations of wines and liquors stored in decanters.*

Home number	Beverage	Approximate duration of storage	Origin of decanter	Pb conc. ($\mu g\ L^{-}$
1	Brandy	5 years	Ireland	7,746
2	Madeira	5 years	Unknown	1,402
3	Scotch	> 3 years	Ireland	2,587
	Port	6–12 months	Sweden	203
	Armagnac	6–12 months	Sweden	472
4	Brandy	> 5 years	Unknown	19,920
	Brandy	> 5 years	Unknown	21,530
	Brandy	> 5 years	Unknown	8,390
5	Gin	6–12 months	Antique, unknown	13
	Brandy	> 1 year	US antique, *ca.* 1830	68
	Grand Marnier	> 2 years	Antique, unknown	173
	Bourbon	18 months	Antique, unknown	17
	Tequila	18 months	Antique, Mexico	300
	Vodka	1 year	Antique, unknown	11

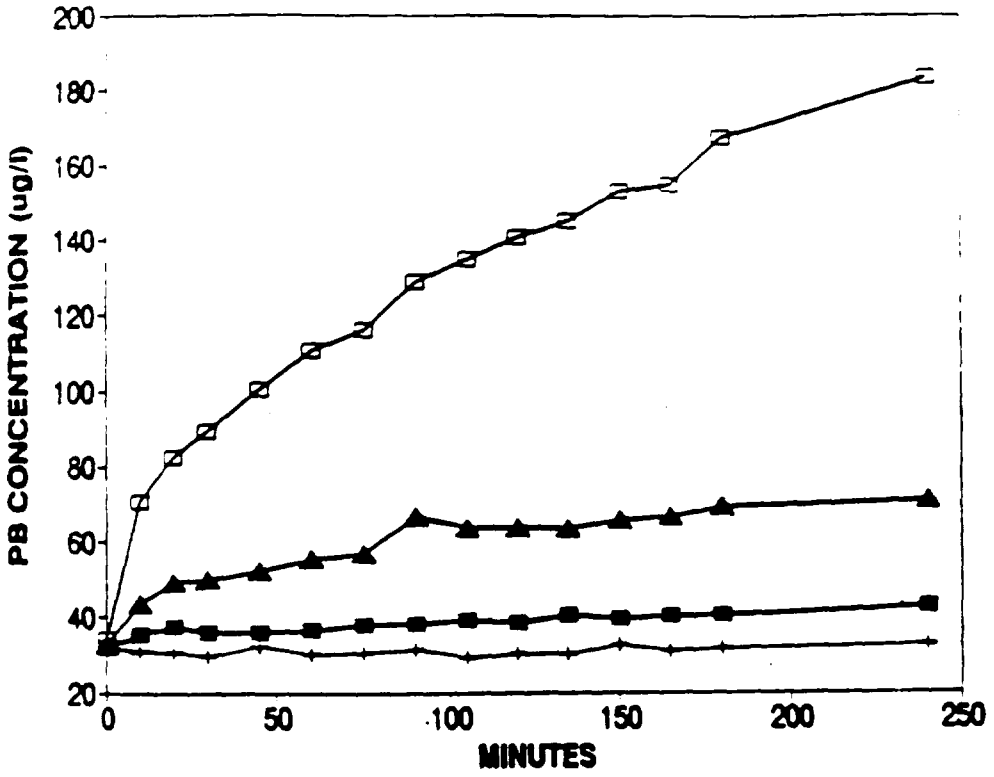

Figure 2. *Mean white wine Pb concentrations (μg L^{-1}) after incubation in four sets of wine glasses (n = 4 glasses/set). Two bottles of California white wine were mixed and 80 mL aliquots were placed in each of 16 glasses. Wine Pb concentrations did not rise in samples placed in a control set of non-lead glasses (+ signs). The Pb concentrations rose steadily in samples placed in Irish (solid squares), French (solid triangles) and Yugoslavian (open squares) lead crystal glasses.*

acid washed with 0.5% Ultrex nitric acid prior to use. We first examined the elution of Pb into apple juice (Gerber Apple Juice with Vitamin C) by pouring the juice directly from the container into all four bottles: 1 mL samples were removed as described above for the wine glass experiment. We then repeated this experiment using infant formula (Enfamil with iron, powdered formula) prepared as it would be at home. Two scoops of formula were placed in each bottle immediately after 120 mL of boiled deionized water had been added; samples for Pb analysis were obtained as above.

Results

The elution of Pb into port wine from three lead crystal wine glasses is illustrated in Figure 1. The Pb concentration of the wine was 89 μg L^{-1} at the time it was introduced into the decanters. After approximately four months, the Pb concentrations reached 5,331, 3,061 and 2,162 μg L^{-1} (mean = 3,518 μg L^{-1}), respectively, in the French, Irish and German decanters. The PbO content of these decanters was stated by the manufacturers to be 32, 32 and 24%, respectively.

We then analyzed the Pb content of alcoholic beverages which had been stored in crystal decanters for long periods of time in the homes of several colleagues. Eleven different decanters had been filled with wines or liquors for six months or more (Table 1). Six beverages from decanters in the first four homes had extraordinarily high Pb concentrations ranging from 1.4 to 21.5 mg L^{-1}. Of interest is the finding that beverages stored in antique decanters in a fifth home were exceptionally low in Pb content. We suspect that these antique decanters pre-date the addition of Pb to crystal glass in the USA.

An experiment was conducted to determine whether lead crystal glasses elute Pb into wine over a short time period. The rises in Pb concentration over time in three different sets of lead crystal glasses are illustrated in Figure 2A–C. Wine Pb concentrations did not rise in wine samples placed in non-lead glasses (Figure 2A). ANOVA revealed a significant rise in Pb over time ($p < 0.0001$). This analysis also showed that each set of glasses had its own elution characteristics ($p < 0.0001$). Furthermore, there was a significant glass-by-set interaction ($p < 0.0001$), indicating that each glass has a characteristic elution pattern. The overall mean ($n = 12$) wine Pb concentration of samples placed in lead crystal rose from 33 μg L^{-1} at the time of pouring, to 68 ± 11 (SEM), 81 ± 15, 92 ± 18 and 99 ± 20 μg L^{-1} after 1, 2, 3 and 4 hours, respectively.

Finally, the elution of Pb from lead crystal baby bottles was examined. Apple juice Pb concentration increased linearly over time in each lead crystal bottle, rising from a mean of 1 μg L^{-1} at the start to 166 μg L^{-1} after four hours. There was no rise in Pb concentration in apple juice placed in ordinary glass baby bottles (Figure 3A). A subsequent experiment examined Pb elution into infant formula. In the lead crystal baby bottles, the mean Pb concentration of the formula immediately jumped to 140 μg L^{-1} after 15 minutes, the continued to rise slowly to 280 μg L^{-1} after four hours (Figure 3B). We surmised that the immediate rise was due to temperature, which gradually cooled during the course of the experiment. We subsequently repeated this experiment under controlled temperature conditions at 20°C, 37°C and 56°C, and observed a temperature-dependent rise in formula Pb concentrations.

Discussion

Lead is relatively ubiquitous in the environment. Baseline Pb intake from sources including air, food, water, beverages and dust has been estimated to be approximately 0.64 μg kg^{-1} day^{-1} in adult females and 0.76 μg kg^{-1} day^{-1} in adult males (Elias, 1985). These values, which do not include exposure to Pb via wine and other alcoholic beverages, correspond to intakes of approximate 40–60 μg PB day^{-1}.

EPA's current maximum allowable level for Pb in drinking

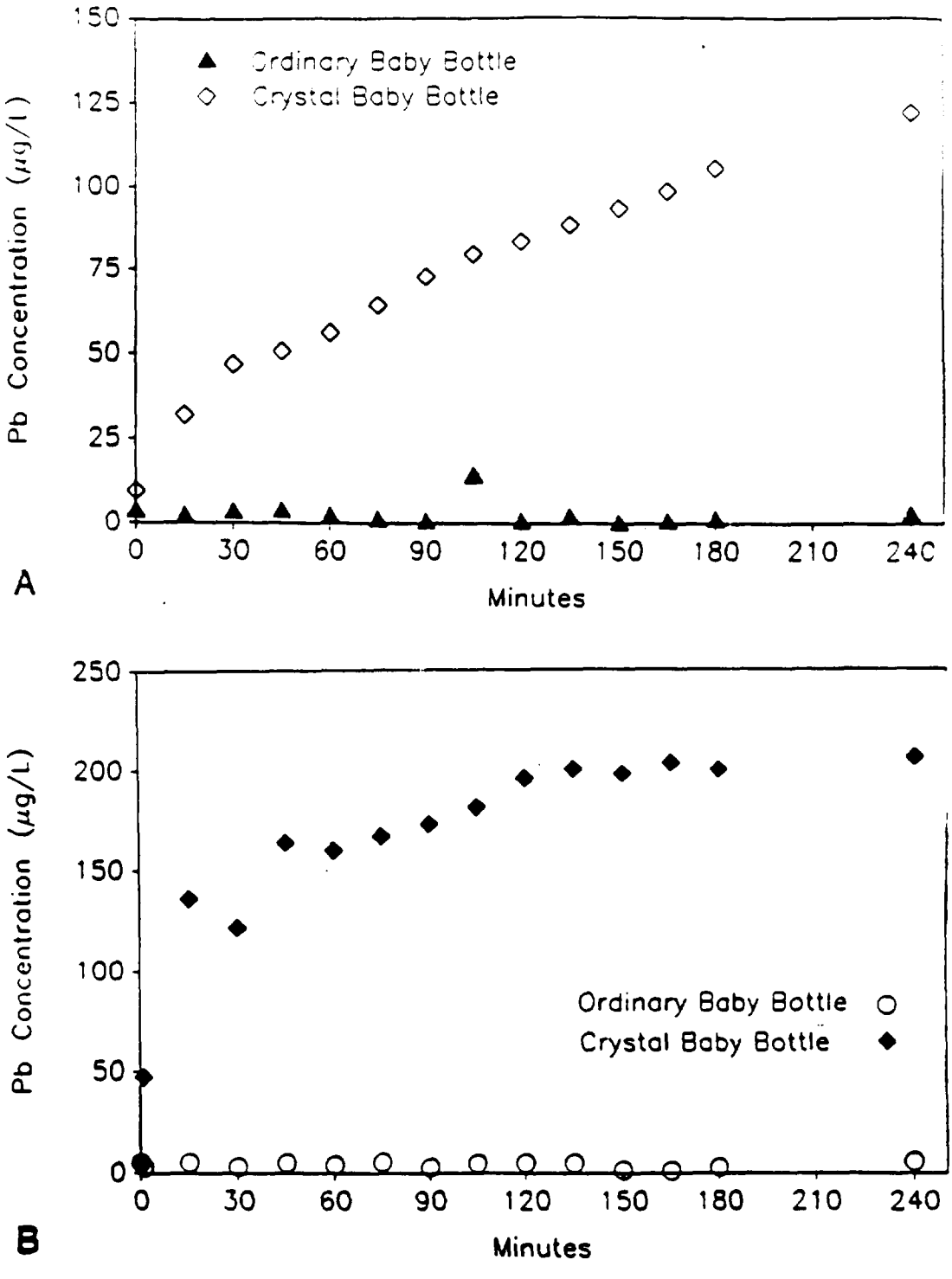

Figure 3 *Mean Pb concentrations (n = 2) rose steadily in apple juice placed in lead crystal baby bottles (open diam Figure 3A) and infant formula (solid diamonds, Figure 3B). No such changes occurred when apple juice (solid triangles. 3A) or infant formula (open circles, figure 3B) were placed into ordinary glass baby bottles.*

water is 50 µg L^{-1}. As a result of recent findings concerning various adverse effects of Pb, it is expected that a revised standard will be more stringent, possibly 20 µg L^{-1} or less (Agency for Toxic Substances and Disease Registry, 1988). For the sake of comparison, Pb concentrations in wines generally range from 30 to 200 µg L^{-1}. Without regard to a possible contribution of lead crystal glass to wine, Elias (1985) concluded that wine does not represent an important so Pb exposure except for those who consume unusuall quantities. Others, however, have concluded that 'regular' wine drinkers, Pb intake from wine may exce from diet, water, air and dust combined (Sherlock *et al.* Smart *et al.*, 1990; Elinder *et al.*, 1988). Indeed, epidemiologic studies have found a dose-response relat

between alcohol consumption and blood-lead concentration (Grandjean *et al.*, 1981; Moreau *et al.*, 1982; Quinn, 1985; Shaper *et al.*, 1982).

The current study indicates that alcoholic beverages stored in lead crystal decanters steadily increase in Pb concentration over time. The findings of our controlled experiments (Figure 1) were confirmed by the analyses of beverages stored in decanters for prolonged periods of time in the homes of our colleagues (Table 1). Indeed, some of the wines stored in lead crystal achieved Pb concentrations of approximately 20 mg L^{-1}, comparable with those estimated for the famous Pb-sweetened wines of Roman times (Nriagu, 1983, 1985). The risk of serious Pb exposure is apparent. Infrequent drinking from a lead crystal decanter would result in intermittent large doses of Pb, while frequent drinking would result in repeated smaller doses of Pb. In either case, we are compelled to recommend that the use of such decanters be modified in some manner, either by labelling or restricting their sale. It is also obvious that the sale and use of lead crystal baby bottles should be banned.

Our short-term experiment with lead crystal wine glasses indicates that Pb begins to elute from the crystal into white wine within minutes. In three sets of lead crystal glasses, each of different geographic origin, wine Pb concentrations rose steadily over a four-hour period of time. While the concentrations of Pb were far less than those observed in the wines stored in lead crystal decanters, the regular use of lead crystal glasses for the consumption of beverages should also be seriously questioned. In particular, because lead readily traverses the placenta (Graziano *et al.*, 1990), pregnant women should probably avoid drinking any beverage from lead crystal glassware.

The current findings agree only in part with those described in a brief letter by deLeacy (1987), who claimed that port wine Pb concentration rose from 0.1 μmol L^{-1} (21 μg L^{-1}) to 5.9 μmol L^{-1} (1,233 μg L^{-1}) after three months of storage in a crystal decanter. That observation is consistent with ours, although we have found stored wines with far higher concentrations. DeLeacy, however, also claimed that the wine Pb concentration reached a plateau after 6–8 weeks of storage, and that wine Pb did not rise during a three-hour incubation in crystal glasses. The data to support the latter conclusions were not presented, nor were the analytical methods, which, in the case of the short-term incubation, may have been too insensitive to detect the relatively small rise in Pb concentration over time.

We can only speculate as to the consequences of the use of lead crystal over the past 300 years. The adverse effects of Pb are well documented and include saturnine gout (Goyer, 1985), as well as effects on blood pressure (Pirkle *et al.*, 1985), the kidney (Goyer, 1985), the erythropoietic system (Cooper and Sigwart, 1980). Prenatal Pb exposure is known to be associated with deficits in cognitive function in later life (Bellinger *et al.*, 1987). The contribution of Pb from lead crystal glass decanters and glasses to adverse health outcomes cannot be precisely estimated at present, largely because the bioavailability of PB in wine is unknown.

Acknowledgement

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Gastro-Intestinal Absorption of Lead in Children and Adults: Overview of Biological and Biophysico-Chemical Aspects

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Abstract

Intake and uptake of lead in the general population is mainly via the gastro-intestinal (GI) tract. Those biological and biophysico-chemical factors operating in the GI tract are the main determinants of Pb bioavailability. They include sites of Pb uptake, the physiology of uptake/transport to blood, the stage of development, interactions of Pb with nutrients, and GI biochemical transformations of ingested material. Lead uptake occurs as ion or complex, from micelles and perhaps by pinocytosis in the infant. Uptake is mainly via the duodenum but other sites can participate, e.g. ileum (pinocytosis) and colon. Transport to blood is by active, carrier-mediated transport and passive diffusion. Uptake may include movement through intercellular tight junctions.

Lead uptake is affected by nutrients in the GI tract, operating synergistically or antagonistically. Iron and calcium interactions are most important and augment those also occurring in vivo in tissues.

Liberation of lead from diverse ingested media, e.g. food, paint, soil and dust, mining waste, is affected by their chemical/physical forms, hydrolytic and oxidative processes in gastric fluid and other GI sites. Such changes in vivo are poorly simulated by in vitro tests. The downward revision of blood lead (Pb–B) levels considered 'safe' to about 0.5 μmol L^{-1} (10 μg dL^{-1}) or lower, causes even sources of moderately bioavailable Pb to become important

Introduction

The concept of biological availability as applied to the public health risks from environmental pollutants is a relatively simple one: potential human health risks associated with a substance are actualized when the substance in a bioactive form is deliverable or delivered to sites of toxic action. The specifics of the delivery are modulated by the many factors discussed in the symposium, including the nature of the lead-containing environmental matrix in sources and pathways.

In areas of nutrition and pharmacology/pharmacokinetics, assessment of a substance's bioavailability has often been the *sine qua non* of research effort and quantitative application. The volume of published work relating to the topic in these disciplines is considerable and growing. Bioavailability is also implicit in that dictum of toxicology which states that 'the dose makes the poison'. The environmental epidemiology of toxic metals and metalloids, by contrast, has often given less attention to circumstances of their form-specific bioavailability and/or bioactivity (*e.g.* Mushak, 1987a, 1985, 1983). This is due in part to the absence of information on form-specific bioactivity and in part to an assumption that the core element should confer uniform toxicity.

Various functional definitions of bioavailability have been put forward and these have as their basis entry into systemic circulation, delivery to sites of action or the extent of some effect.

A generic form of the definition by Firsov and Prokovskii (1986), put forth for drugs, is useful:

"The biological availability is the fraction (nutrient, drug or human environmental toxicant) of substance entering the systemic circulation (extent of systemic absorption) and the rate at which entry occurs."

The bioavailability of environmental lead in human populations is defined by the biological aspects of lead uptake from body compartments, the biophysico-chemical behavior of different lead species in body compartments, interactive relationships of lead with other species in body compartments and toxicokinetics of lead in the human body. We are here concerned with intake/uptake of exogenous lead, but it should be kept in mind that release of lead from the body stores such as the skeleton produces bioavailable lead and exogenous lead exposure.

How does one determine lead bioavailability, particularly ingested lead, in human populations? Approaches include: (1) use of appropriate experimental animal models to simulate the behavior of lead species in humans; (2) validated multimedia toxicokinetic models using appropriate intake/uptake kinetic parameters; or (3) epidemiological approaches through biological monitoring, including methods of inferential statistics for identifying relationships of biological markers to lead sources or pathways.

Bioavailability of lead in the gastro-intestinal (GI) tract of humans and experimental animals is of particular interest, since

† *Special issue incorporating the Proceedings of the Symposium on the Bioavailability and Dietary Exposure of Lead.*

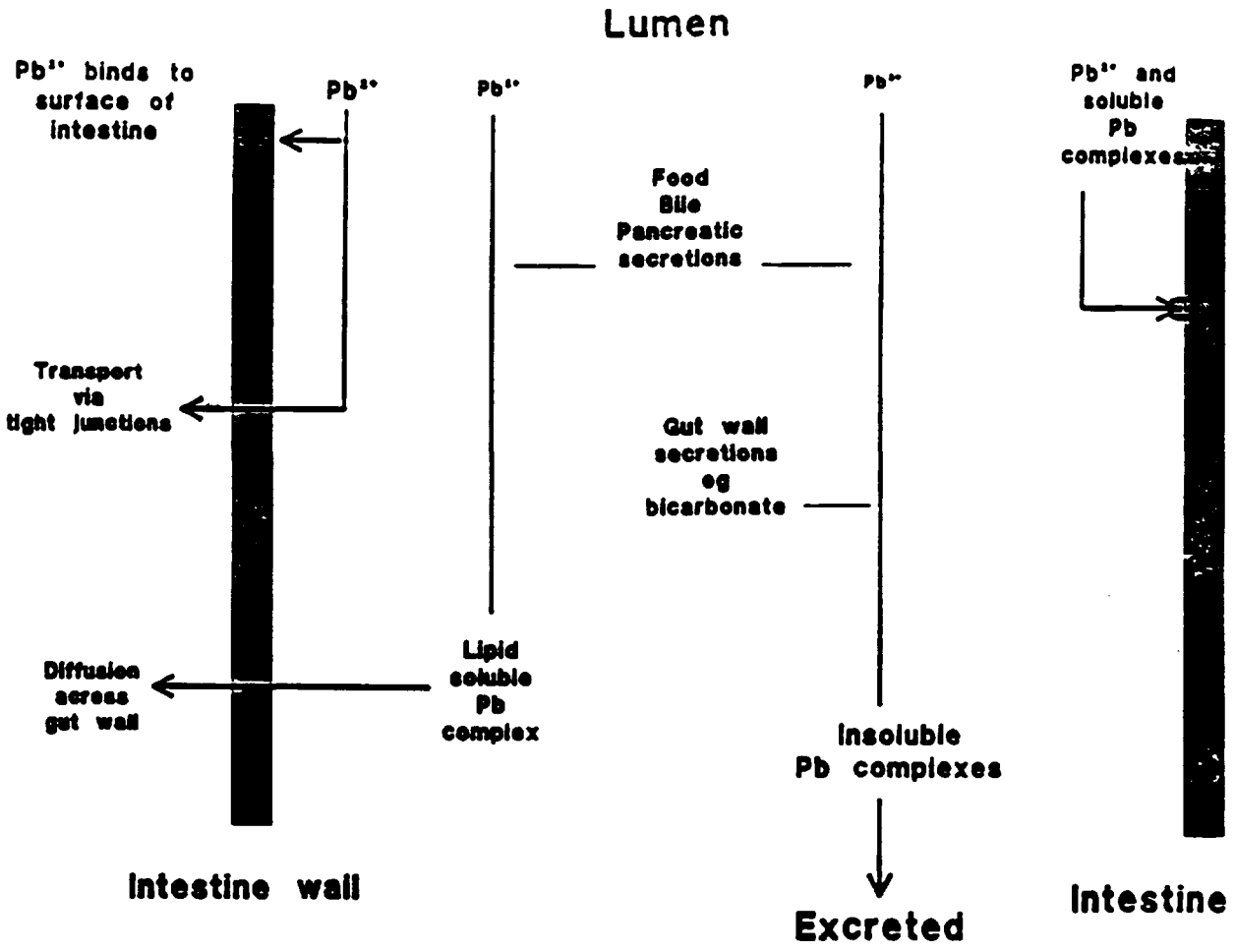

Figure 1 *Schematic diagram of intracellular/inter- cellular lead uptake by enterocytes in the human small intestine. a ++ charge within/between cells are either hydrated or interacting with ligand sites during diffusion.*

ingestion is the major route of lead exposure for most risk segments of the general population. The enteric bioavailability of lead in some ingested medium, in turn, is governed by various intrinsic (biological and biophysico-chemical) or extrinsic (level of source-specific exposure) factors which can operate separately or in combination.

Biological Determinants of Human GI Absorption of Lead

Biological determinants include: (1) interspecies differences, *e.g.* ruminant *vs* monogastric species such as humans; (2) the site of lead uptake in the GI tract; (3) the physiological and molecular processes underlying lead uptake and transport to the systemic circulation from the gut; and (4) the stage of physiological development, *e.g.* children *vs* adults and young/middle-aged adults *vs* the aged.

Interspecies differences in the GI absorption of lead

Interspecies differences in the enteric and metabolic handling of xenobiotics have principally been of interest in the organic chemical substances (Calabrese, 1984; Ral Smyth, 1960), with particular reference to dist attributable to mixed function oxidase (MFO) transfo of various substances. Comparatively less has been fort with regard to metals and metalloids (Calabrese, 198 relevant comparisons have appeared for arsenic and and certain forms of mercury (Mushak, 1985, 1983) b less for inorganic, divalent lead, the most environ significant chemical form (see, however, Scharding anc 1973 and relevant papers in these Proceedings).

Any effect of species on lead bioavailability woul on differences in such parameters as GI tract anat physiology, gastric processing of lead-bearing media, acidity and/or oxidation–reduction potential participation of biliary clearance. Existence of dependent differences, in turn, becomes a key consid the development of animal models of lead bioavail human populations. Specific discussions of animal n

Table 1 *Studies of lead uptake sites in the mammalian GI tract.*

Species	Dosing details	Results	Reference
In vivo			
Male Wistar rats	*In situ* ligated intestinal loops injected w/Pb–203	Pb uptake primarily in duodenum	Conrad and Barton, 1978
Sprague-Dawley suckling rats: 10, 14 and 24 days old	GI intubation w/Pb–203 followed by segment radiography	Duodenum is site of PB uptake w/transport, transport, ileal uptake w/retention at 24 days	Henning and Leeper, 1984
Same: 9–16 days old	GI intubation w/Pb–203 as salt or in milk micelles	Pb salt absorbed in duodenum, Pb in micelles absorbed in ileum	Henning and Cooper, 1988
3–4 week-old White Leghorn chicks	Pb–203 injected into situ ligated intestinal loops, different diets	Label uptake in duodenum varied w/level of nutrients	Edelstein *et al.*, 1984
C56 Bl/6 Jax adult mice	Pb–203 given via open-ended duodenal loop perfusion	Duodenal uptake, variable with iron status	Flanagan *et al.*, 1979
Adult guinea pigs	PB–Oac in drinking water	Pb uptake in ileum and colon, similar tissue levels	Rizzi *et al.*, 1989
Adult guinea pigs	Dosing of isolated loops, colon and jejunum w/Pb solution	Jejunal uptake higher than for colon; other sites not tested	Hussein *et al.*, 1984
In vitro			
Adult Wistar rats	Everted duodenal sacs incubated w/Pb–210	Label uptake and transport, mucosal to serosal surfaces of duodenum	Barton, 1984

lead bioavailability in humans are presented elsewhere in these Proceedings.

There is little evidence to support any notion that ingested lead behaves differently in ruminants compared to monogastric animals, whatever the differences in gastric anatomy and physiology. For example, regurgitation and chewing of lead-containing material and a methanogenic, chemically reducing milieu in the ruminant GI tract might be expected to affect lead bioavailability differently than when simple passage of ingested lead through the monogastric stomach and intestines with an oxidative environment occurs.

On the other hand, there is extensive literature documenting that ruminants readily absorb lead from contaminated range feed/soil and experimentally-dosed diets (*e.g.* Allcroft, 1950; US EPA, 1986; Zmudzki *et al.*, 1986) and are at rather high risk for lead poisoning (Allcroft, 1951; Hammond and Aronson, 1964; Zmudzki *et al.*, 1986). This vulnerability possibly reflects soil ingestion during grazing. Furthermore, Stara (1971) has reported that the extent of GI uptake of elements such as cesium by the ruminant (80%) is not much lower than monogastrics (90%). These Proceedings discuss the topic elsewhere.

Sites of uptake of lead

The epithelial lining of the small intestine in humans and experimental animals is the principal anatomical and physiological locus of uptake and transport from the lumen. There also is evidence for the involvement of colonic epithelium in experimental systems. The stomach separately plays a role in uptake via transformation(s) of lead-bearing media or form- specific lead to potentially more soluble or otherwise mobile forms.

Uptake involves epithelial cells on the mucosal surface, the enterocytes. These specialized cells are structured with finger- like projections, the microvilli (Figure 1). Such morphology provides an enormous surface for contact with and uptake of lead and other substances relative to cellular volume and time in the gut. Note in Figure 1 the intercellular junction and associated intercellular lateral space, which also may participate in lead transport.

Various *in vivo* and *in vitro* studies have been done to identify the site(s) of uptake and transport of lead, and the more significant reports are summarized in Table 1. It is important to keep in mind that these data were gathered typically by using surgically and physiologically manipulated segments of the GI tract in experimental species. The full extent to which these manipulations introduce artifacts in the results is not known.

In rats and other species, lead uptake and transport principally occurs in the duodenum in developing and mature animals (Henning and Cooper, 1988; Barton, 1984; Edelstein *et*

Table 2 *Studies of lead uptake sites in the mammalian GI tract.*

Species	Dosing details	Results	Reference
In vivo			
Adult and suckling Sprague-Dawley rats	Oral intubation or drinking H_2O; Pb dose range of 1–100 mg kg^{-1}	Concentration-dependent uptake rates were observed, *i.e.* carrier transport and saturation kinetics	Aungst *et al.*
C56 Bl/6 Jax adult mice	Open-ended, *in-situ* perfusion, Pb–203 or Pb–210 + carrier	Uptake dependent on lumen Pb, *i.e.* saturation kinetics	Flanagan *et al.*
White Leghorn chicks	*In vivo*, ligated duodenal loops, injected Pb–203 + carrier, 0.01–1.0 nM Pb	Concentration-dependent Pb uptake; saturation kinetics	Mykannen and Wasserman
Suckling Sprague-Dawley rats	*In vivo* intubation of Pb–203, as salt or in milk micelles, segmental analyses of intestinal tract	Pb in micelles absorbed only with retention in ileum, Pb salt absorbed in duodenum with transport	Henning and
In vitro			
Adult Wistar rats	Rat everted gut sacs with Pb–210 in bathing medium, active transport inhibitors	Duodenal sacs transported Pb, by active transport. Ileal and jejunal sacs did not transport Pb	Barton
Adult and juvenile Sprague-Dawley rats	Everted gut sacs with Pb ion at 0.5–48.3 μM, metabolic inhibitors	Non-linear Pb uptake *vs* dose, active transport dominant at all doses, with diffusion <20%	Aungst and
Adult rats	Everted gut sacs with Pb ion. Cellular Pb localized by histochemical techniques	Pb appears localized between enterocytes, in 'tight junction' region	Coogan and Morton *et al.*

al., 1984; Henning and Leeper, 1984; Flanagan *et al.*, 1979; Conrad and Barton, 1978). In general, the more reliable *in vitro* data support *in vivo* results, *i.e.* uptake via duodenum (Barton, 1984). In other studies experimental artifacts, such as the use of medium cofactors that remove lead by precipitation, limit conclusions to be drawn about regional uptake in the small intestine (*e.g.* Blair *et al.*, 1979; Gruden and Stantic, 1975).

Hussein and coworkers (1984) have found that lumenal lead dosing of isolated loops of guinea-pig colon and jejunum yields significant lead uptake at both sites, but colonic uptake is less than that in jejunal epithelium. The relative amount of lead actually entering the bloodstream from transcolonic transport was not determined. However, Rizzi *et al.* (1989) reported that orally dosed guinea pigs showed tissue levels of lead in colonic tissue similar to those in ileum.

In theory, xenobiotic transport from the gut to the circulation can entail such processes as carrier-mediated transport, passive and facilitated diffusion, pore filtration, phagocytosis and pinocytosis (Calabrese, 1984). In the case of lead, a number of these mechanisms have been identified. Various studies of the kinetic nature of lead movement from the intestinal lumen to the bloodstream are presented in Table 2.

Transport of lead from duodenum to the blood stream appears to include significant intracellular uptake via active transport system that normally functions nutrients, such as calcium and iron, with further passive diffusion being reported (*e.g.* Flanagan *et* Barton *et al.*, 1978).

Evidence for carrier-mediated transport observation of energy requirement and identific proteins (*e.g.* Henning and Cooper, 1988; Bart Mykannen and Wasserman, 1981) and saturability o indexed as loss of tissue lead linear response above level of oral dosing (Aungst and Fung, 1981; Flana 1979).

There is also evidence that paracellular uptake diffusion through 'tight junctions' will occur, bas everted sac techniques and histochemical staining. tight junctions have a pore diameter of 10–16 Å, charge density and high selectivity for cations (*e.g.* *al.*, 1985; Coogan, 1982).

Is this mode of uptake an artifact of experimen co-existence with intracellular transport *in vivo* but n cationic (*vs* complexed) lead? The latter is the more supporting information from data on other ionic met

It is known that some uptake of iron, in low

Table 3 *Relationship of age and development to GI absorption of lead.*

Study group	Study details	Results/comments	Reference
Humans			
8 children, aged 3 months to 8 years	11 lead balance studies	Mean extent of Pb uptake was 53%	Alexander *et al.*, 1973
12 infants, aged 2 weeks to 2 years (2 studies)	Two-part lead balance studies: *Part 1:* 51 studies with 9 children	42% absorption	Ziegler *et al.*, 1978
	Part 2: 38 studies with 6 children	42% absorption	
29 hospitalised children, aged 3 weeks to 14 years	Lead balance studies: 104 studies with 29 children	Showed highly variable uptake, 15 children in negative balance, w/ –40% uptake. Results limited by unknown Pb exposure and stresses of disease and injuries, *e.g.* bone fractures	Barltrop and Strehlow, 1978
Animals			
Sprague-Dawley suckling rats	Intubation of Pb–203 at varying doses as salt or in milk micelles	Ileal uptake of lead with retention is greater than elsewhere in gut	Henning and Cooper, 1988
Albino rats: 1–2 week-old sucklings; 6–8 week-old weanlings	GI administration of Pb–203 and measurement of label	1 week-old animals absorb 70% lead *vs* 23% in weaned rats	Kostial, 1987
Fisher–344 rats: adult (8 months) and old (16 months)	Oral Pb disposition at 0, 250, 500 ppm Pb in drinking water	Marked changes in bone and soft tissue Pb of old rats; Pb–B was similar	Cory-Schlecta, 1990a
Fisher–344 rats: young (21 days); adult (8 months) and old (16 months)	Oral Pb disposition at various doses: 0, 2 or 10 mg Pb kg^{-1} day^{-1}	Changes in old rat bone and excreted lead; no change in GI uptake	Cory-Schlecta, 1990b
Fisher–344 rats: adult (8 months) and old (16 months)	Oral Pb disposition at 50 ppm Pb in drinking water	Increases in Pb–B and soft tissue Pb in old rats; may reflect higher uptake	Cory-Schlecta *et al.*, 1989

weight forms, is through passive diffusion and occurs via tight junctions (Simpson *et al.*, 1989) while aluminum is normally transported via tight junctions (Provan and Yokel, 1988). Furthermore, aluminum uptake is markedly enhanced by citrate in animals and humans (Slanina *et al.*, 1986; Froment *et al.*, 1989a), while citrate imparts a similar enhancement of lead absorption (Spickett *et al.*, 1984). Froment *et al.* (1989b), using ruthenium red and Ussing chamber techniques, have shown conclusively that citrate functions in aluminum uptake by opening tight junctions for more facile aluminum passage.

Age and developmental determinants of GI lead absorption in humans and animals

It is now known that age and the stage of development in humans and experimental animals have an intrinsic effect upon body lead burdens. These closely linked factors potentially operate through a variable combination of: (1) the extent of lead uptake in the GI tract; (2) the distribution of lead among tissues and its retention; (3) the relative efficiency of excretion of absorbed lead.

In examining this body of data, it is important to understand the nature of the techniques for assessing the above inter-related phenomena with respect to distinguishing among higher uptake, higher retention and relatively lower extent of excretion. One should also understand that higher uptake in intestinal epithelium does not necessarily result in more lead delivered to the blood. These distinctions have not always been comprehended by various investigators. We are mainly concerned here with age and development as a factor in more lead uptake from the GI tract, and this topic has been reviewed

Table 4 Various nutrient relationships with lead in humans.

Group	Study design	Results*	Reference
All nutrients			
Adult volunteers (n = 23)	Ingestion of Pb–203 label variably timed with meals	Minimal uptake of 61% Pb with fasting, 4% uptake with meals. Intermediate uptakes between these times	James *et al.*, 198
Calcium			
Cluster sampling of 1–11 year-old children in NHANES II (n = 2926)	Statistical analyses of Ca in diet *vs* Pb	Dietary Ca inversely related to Pb–B. (p = 0.028)	Mahaffey *et al.*, 1
Infants (see Table 3)	Statistical analyses of dietary Ca and Pb uptake in balance studies	Pb uptake inversely related to diet Ca; occurs even within Ca RDA guidelines	Ziegler *et al.*, 197
Children 1–6 years old (n = 43)	Statistical analyses of dietary Ca and Pb–B	Ca intake and Pb–B were negatively correlated (r = 0.327; $p < 0.05$)	Johnson and Tene 1979
Adult volunteers (n = 8)	Pb–203 label uptake in Ca/P–variable diets	In fasting, 60% Pb uptake, with Ca + P giving 10% uptake	Heard and Chamt 1982
Iron			
Children 2–6 years old in NHANES II survey (n = 1677)	Statistical analyses of Pb *vs* EP as a function of Fe a function of Fe	Dose-effect curves for EP *vs* Pb–B showed slope depends on % transferrin saturation	Marcus and Schw 1987
Children at high risk for Pb toxicity and Fe deficiency	Analyses of relationship of Pb–B to EP and Fe deficiency	Children with Pb–B >1.5 μmol L^{-1} and elevated EP had increased rate of Fe deficiency	Yip *et al.*, 1981

EP = erythrocyte protoporphyrin.
* 1 μmol L^{-1} Pb–B = 20 μg dL^{-1}.

(Musak, 1989; US ATSDR, 1988; Kostial, 1987; US EPA, 1986). Some of the relevant studies are presented in Table 3.

The main focus of this area has rightfully been on the growing child. Also, there may be a role played by the ageing GI tract in lead toxicokinetics. While the latter is only now being examined to any extent, the ageing of populations in developed countries, especially in the United States, and the problem of potentially mobilizable lead after life-long body accumulation requires much more attention to the matter. Available data are included in Table 3.

Young children, in those studies where reasonably stable exposure histories can be assumed to have existed (Ziegler *et al.*, 1978; Alexander *et al.*, 1973), have been shown to absorb (and also to retain) more ingested lead than do adults, 40–50% *vs* 10–15% in adults. The data of Barltrop and Strehlow (1978) are based on hospitalized children with fully unknown lead exposure histories and who have metabolic stresses of disease and trauma, *e.g.* bone fractures, and are not easily interpreted. Many studies comparing developing *vs* adult experimental animal models show the same phenomenon (Mushak, 1989; US ATSDR, 1988; Henning and Cooper, 1988; Kostial, 1987; US EPA, 1986), and animal models of bioavailability mu account of this.

What is the physiological basis for enhanced lead in young (pre-school) children and suckling animals? pre-school children are more apt to be at risk for n deficiencies which can enhance lead uptake, as discussed the nature of the studies of Ziegler *et al.* (1978) and Ale *et al.* (1973) would tend to minimize any nutritional fact example, Ziegler *et al.* used a middle-class infant co which deficiencies were apt to be minimal, while Alexa *al.* used a broad range of children, only some of whom the deficiency-risk group.

In the rat, many of the structural parts of the small in are matured at weaning, including villus and crypt (Trehair, 1989). Furthermore, the well-known g phenomenon of pinocytosis in the suckling rat ileur Williams and Beck, 1969) has also been identific significant factor in increasing suckling animal uptake in the gut. This involves ileal pinocytosis of lead micelles (Henning and Cooper, 1988). Once pinocytose lead remains sequestered in the cell, and can be cou

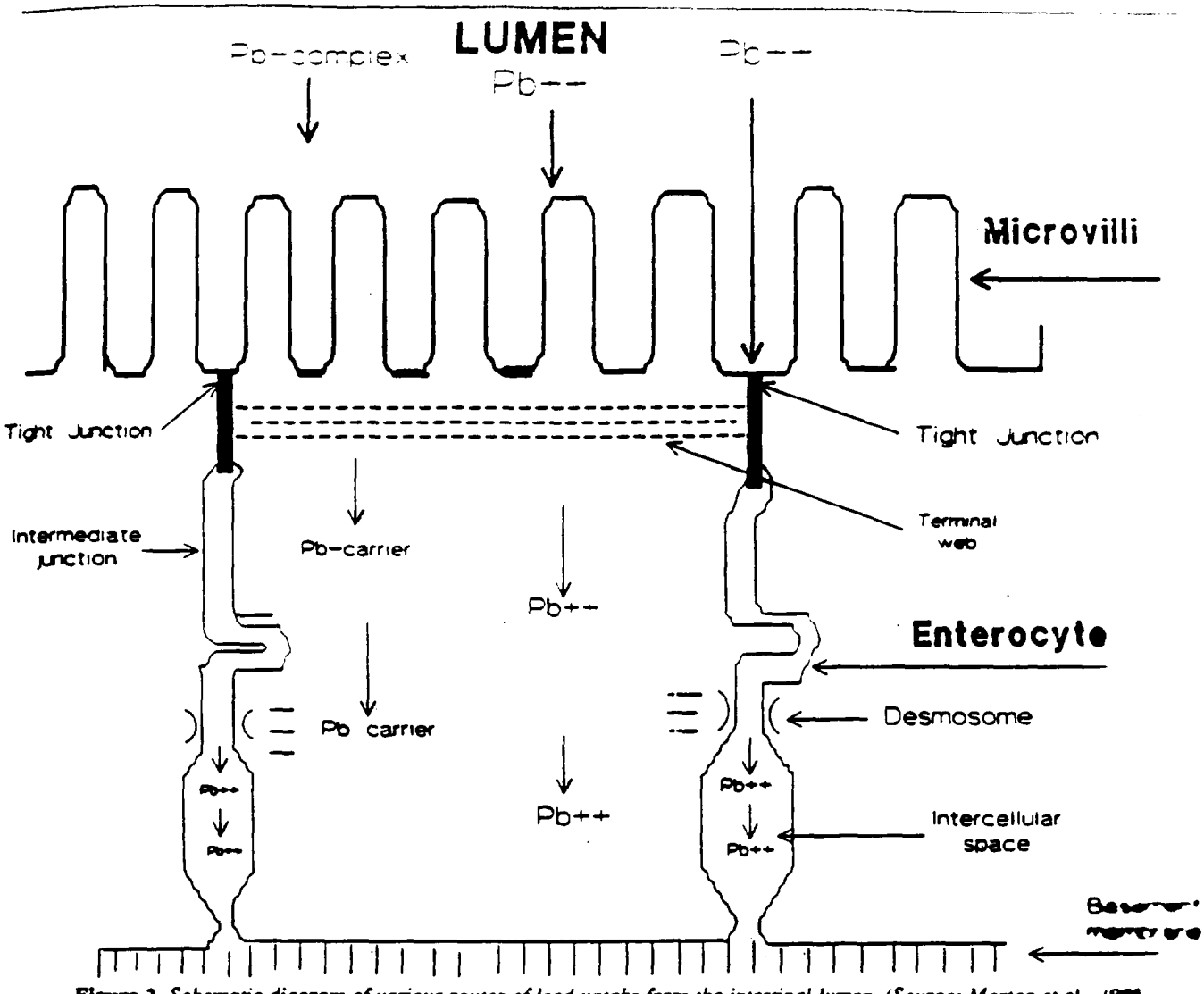

Figure 2 *Schematic diagram of various routes of lead uptake from the intestinal lumen. (Source: Morton* et al. *19[illegible]*

contributing to body retention without necessarily contributing to lead in blood. Epithelial desquamation then results in simple elimination. Consequently, such uptake does not translate to more lead entering the general circulation.

The level of ontogenic concordance in gut maturation between humans and animals in the neonate and suckling period is not high, inasmuch as the human newborn starts life with a more mature GI tract than the neonate rat (Henning, 1987). On the other hand, acid and pepsin production rates in children do not approximate adult levels until about two years of age (Christie, 1981; Deren, 1971), and some food proteins may be more readily taken up in infancy than later, suggesting a pinocytotic mechanism (Walker, 1985; Henning, 1987).

Limited information exists on changes in Pb uptake in the ageing mammalian GI tract. In human populations there appears to be a modest falloff of lead body burden owing to either metabolic or dietary changes (*e.g.* US EPA, 1986) after age 60. The post- menopausal female segment actually shows an increase, probably due to bone mineral changes and enhanced bone lead resorption (Silbergeld *et al.*, 1988). In the ageing rat, oral dosing at 50 ppm lead is associated with an elevated blood lead level compared to the younger adult, but this difference does not persist at higher dosings (Cory-Slechta *et al.* [illegible] Cory-Slechta, 1990a). These studies suggest that ageing may affect tissue lead distribution and lead excretion more than GI uptake (Cory-Slechta, 1990a,b; Cory-Slechta *et al.*, [illegible]

Interactive-relationships of lead in the GI tract

Lead absorption from the GI tract of humans and experimental animals is markedly affected by the presence or absences of other bioactive agents in the gut, particularly certain classes of nutrients (Mushak, 1987b; US EPA, 1986; Mahaffey, 1982). Such interactions augment those which occur elsewhere within the body and help to define overall lead toxicokinetics and lead toxicity in humans.

An integrated expression of such interactive behaviour is the full diet effect, as seen by the impact of meal scheduling on lead uptake in the human gut. James *et al.* (1985), using human volunteers ingesting labelled lead (Pb–203), found that when a meal was taken 12 hours before tracer lead ingestion, label retention was about 62%. A similar percentage was found when meals were consumed seven hours after label ingestion on an empty stomach. Shorter periods of label–meal separation gave intermediate retentions, while the lowest retention, about 5%,

Preparation	Subjects	Outcome*	Reference
Surma	Case report	Severe Pb poisoning with encephalopathy	Warley *et al.*, 1968
Surma	Asian children (n = 37) using 'surma' *vs* Asian controls (n = 25)	Mean Pb–B = 1.7 μmol L^{-1} for 'surma' children *vs* 1.0 μmol L^{-1} for controls	Ali *et al.*, 1978
Surma	Asian children using 'surma' *vs* controls	Significantly elevated mean Pb–B over control Pb–B	Green *et al.*, 1979
Al kohl	Kuwaiti infants <6 months old (n = 4)	Acute Pb poisoning	Fernando *et al.*, 1981

* 1 μmol L^{-1} Pb–B = 20 μg dL^{-1}.

occurred with co-ingestion of meal and label. These results are in accord with a number of other studies showing the inverse link of lead uptake with levels of nutrients in the gut.

There are various categories of lead interactions applicable to GI behaviour of lead. While these can entail toxicant–toxicant interactions to some extent, attention has mainly been on lead–nutrient interactive behaviour. Interactions can be synergistic, additive or antagonistic, and in some important cases intrinsically antagonistic agents can appear to function extrinsically in a synergistic way due to their deficiencies during lead exposure, *e.g.* calcium–lead interactions.

There are many interactions with lead in the GI tract that have been described in the literature (see US EPA, 1986), but some have more obvious and recognized impacts on public health risk than others (Table 4). Two nutrients that figure prominently are calcium and iron. Phosphate and vitamin D metabolites are also important, but are not as fully characterized epidemiologically. Lead interactions with zinc, protein, fats, saccharides and natural chelators are known principally from studies in experimental animals.

A number of lead exposure populations have been studied in terms of calcium status and its effect on such measures as blood lead. This includes relevant data in the large and comprehensive Second National Health and Nutrition Examination Survey (NHANES II). Mahaffey *et al.* (1986) reported a statistically significant inverse association between dietary Ca intake and blood lead using data gathered in the NHANES II. This large analysis is consistent with balance study results of Ziegler *et al.* (1978) for infants and various investigations of the interactive relationship in high-risk children (Johnson and Tenuta, 1979; US ATSDR, 1988) and adult volunteers (Heard and Chamberlain 1982).

Numerous animal studies have described the quantitative and mechanistic aspects of Pb–Ca interactions in the mammalian gut, and these have been reviewed (US ATSDR, 1988; Mushak, 1987b; US EPA, 1986; Mahaffey, 1982). Mechanisms of interaction in the gut include a ternary interaction of Pb, Ca and phosphate (Heard and Chamberlain, 1982; Smith *et al.*, 1978) and competitive uptake of Pb on Ca carrier protein (Barton *et al.*, 1978), which would be an saturable transport process (see above). That the interaction is a robust one can be seen in the study of *et al.* (1978) where an inverse correlation of absorbed Pb intake was seen at intake levels of Ca within the recommended daily intake.

The large NHANES II database has also been examined terms of Pb–Fe interactions in children at the age of deficiency. Iron status has been shown to be to blood lead, *i.e.* iron deficiency is associated with higher lead levels in this survey (Mahaffey and Annest and Schwartz, 1987). Other reports showing this and involving high-risk children have appeared (e.g. Yi 1981).

As with Ca, a number of animal models of the interaction have been described in which Fe defi produces increased Pb uptake/retention. The Fe–Pb is quite complex mechanistically, but it can be deficiency stimulates iron absorption and this enhances Pb uptake via site binding at intestinal recep the nutrient (Morrison and Quarterman, 1987).

Are the lead–nutrient interactions metabol reciprocal, *i.e.* do alterations in levels of enteric lead nutrient metabolisms in the same way as the reverse. simple glance, they might be expected to do so but they a and for a good reason. Lead is non-essential and xenc while elements such as iron, calcium, *etc.*, are essential n under tight homeostatic control. It is reasonable xenobiotic agent can 'piggy-back' on one part of the homeostatic control pathway for nutrients, as in Pb bin carrier proteins in nutrient deficiency. Fully reciprocal bc would require that Pb effectively obliterate tight home control of nutrients, something which is highly unlikely a than very high Pb exposures. Lead would, therefore, robust in affecting Ca or Fe uptake than the reverse.

This may explain why deficiencies in Ca and Fe e Pb uptake but the enhancement does not persist linear repletion or excess (*e.g.* Mahaffey-Six and Goyer, Morrison and Quarterman, 1987). Homeostatic c applicable to adequate or excess, rather than inade

nutrient is operative, whatever the level of Pb present. Furthermore, Pb can function to alter Ca metabolism in ways other than direct, reciprocal interaction. Fullmer and Rosen (1990) found that Pb affects Ca metabolism prior to calbindin D synthesis via the cholecalciferol system in experimental animals.

Overview of biological factors in GI uptake of lead

One can conclude that there are different mechanisms for GI uptake of lead in humans and experimental animals, and these are graphically summarized in Figure 2. As summarized by Morton *et al.* (1985), uptake of lead can include participation of the soluble, divalent Pb cation or various soluble complexes. Simultaneously, some sizeable fraction of divalent lead ion will be forming relatively insoluble, excretable lead complexes, *e.g.* hydroxide, bicarbonate or phosphate/mixed phosphate. Maturity of the GI tract and nutrient interactions affect these processes.

Uptake of lead ion by paracellular means, *i.e.* diffusion through 'tight junctions', has been shown in one study to be a major route under certain experimental conditions (see above). There is supporting evidence for this in other studies of elements and their interactions with 'tight junctions'.

Intracellular lead uptake is the route that has been studied and most accepted as the principal pathway in experimental systems. Such uptake is consistent with saturable, active transport as well as some passive diffusion. Diffusion most likely involves a neutral complex or other lipophilic form. Binding of lead ion to receptors in the enterocyte that serve for active transport of Fe and Ca would account for active transport. This dual mechanism of uptake appears to be one explanation of the non-linear nature of the relationship of lead dose in the GI tract and lead in blood or other biological marker.

Biochemical/Biophysical Factors in the GI Absorption of Lead

Some biophysico–chemical factors which affect the GI uptake of lead in human populations are of importance, and they include GI solubility, particle size and reactivity of the ingested lead- containing chemical matrix with reference to *in vivo* mobilization. These factors are not intrinsically biological but they operate within, and interact with, the biological uptake/intake compartments to affect bioavailability.

These factors take on added importance when one considers the chemically and physically diverse exposure media ingested by populations at risk: tap water, beverages, baby foods, adult diets in general, lead in urban dusts and soils arising from input from mobile emissions, paint and stationary sources, lead in communities impacted by lead production and use, *i.e.* secondary and primary lead smelter emissions and tailings from ore milling, lead battery plants, *etc.*

In vivo bioavailability versus in vitro behavior

One factor of concern in the GI handling of lead is the extent to which lead can be dissolved or otherwise mobilized with the ingestion of certain media, and movement to the stomach and small intestine. This especially applies to lead in those chemical forms considered to be inert by typical *in vitro* reactivity criteria. For example, it is important to keep a distinction between lead mobilization from media in the human stomach and simple solubility tests intended to simulate such complex activity. The latter are relatively crude simulations of events *in vivo*, given that the human stomach harbours significantly basal acidity, has a large capacity for sustained acid output in response to stimulation by acid-consuming ingested material, and may have, in its gastric fluid, substances other than just hydrochloric acid which can interact with the lead ion (see below)(Merki, 1988; Konturek, 1981; Davenport, 1977; Connell, 1974).

The resting pH of the gastric fluid in children is about 1 (Connell, 1974), while sustainable gastric acid output with stimulation can approach 150 mequiv L^{-1}, depending on such factors as the gastric oxyntic (parietal) cell mass (Konturek, 1981; Davenport, 1977). In addition to gastric HCl there are zymogens (trypsinogen, pepsinogen, renninogen), trypsin, pepsin, rennin and electrolytes (*e.g.* Davenport, 1977).

The complex interactions of the GI tract with lead can be illustrated in the *in vivo* behaviour of various chemical forms of lead. Lead sulphide, a chemical form of lead considered less bioavailable than the chloride, sulfate, or organic chelates, has a simple solubility product constant (Ksp) of 3.4×10^{-28} but is extensively solubilized by acidic gastric juice to lead chloride, $Ksp = 10^{-4}$ (Healy *et al.*, 1982). Such reactivity towards gastric juice probably plays an important role in the reported bioavailability of this species, particularly when used in ethnic preparations such as the (conjunctival) eye cosmetic known as 'surma' in Asia and 'al kohl' in the Middle East. As noted in Table 5, the sulfide in such preparations has been documented as causing elevation of blood lead to toxic levels (*e.g.* Ali *et al.*, 1978; Green *et al.*, 1979) and overt lead intoxication (Warley *et al.*, 1968; Fernando *et al.*, 1981).

Interestingly, 'surma' is Urdu for antimony and this metalloid was the element historically used in the sulfide preparation. The recent change to lead for economic reasons accounts for the rather recent history of toxicity risk associated with the use of this cosmetic preparation.

Several studies of lead isotope uptake in the human gut have been done and these indicate that the sulfide can have measurable or comparable bioavailability to that of forms considered much more soluble. Rabinowitz *et al.* (1980) found that lead as the sulfide, when ingested during meals or in fasting, was absorbed to the same amount as the lead chloride or cysteine complex. In fasting, there was 35% uptake for all three forms. Chamberlain *et al.* (1978) found that the sulfide was absorbed to the same degree as the chloride with meals, but less in fasting. The difference with fasting conditions for the sulfide in the two studies may reflect differences in particle size of the sulfide (see below).

Particle size and bioavailability of lead

Particle size of lead-bearing media is an important factor in the enteric mobilization of lead. Available experimental data indicate that the smaller the particle, the more easily it will be dissolved in the stomach or elsewhere in the GI tract.

Barltrop and Meek (1979) reported that particle size of lead in several forms was a significant determinant of blood lead in rats fed the toxicant. The smaller the particle, the higher the blood lead level. The most pronounced effect was seen with metallic lead, indicating that relative ease of both oxidation to the divalent state and dissolution were factors of importance.

[illegible] found that the extent of lead sulfide solubility in gastric juice *in vitro* was inversely proportional to particle size, particles of 30–μm diameter being much more soluble than like material of 100–μm diameter. According to Healy *et al.* (1982), lead sulfide was found in cosmetic preparations (see earlier discussion) in particle sizes ranging up to 100 μm. Since the sulfide-based cosmetics, whatever the particle sizes, all appear to be associated with elevated blood lead and/or toxicity risk (see Table 5), the cosmetics with 100–μm particles of lead sulfide contain relatively bioavailable lead. A sulfide particle size of 100 μm is also within the range of concern for general bioavailability of lead encountered in lead-bearing dust and soil media. Theoretically, as particle size decreases, the Noyes-Whitney dissolution law dictates that the substances will become fully soluble at a sufficiently small mean diameter (Healy, 1984).

These laboratory data augment extensive epidemiological and environmental evidence pointing to the importance of particle size of lead-containing media. First, diverse studies document increased lead absorption in children in urban (Bornschein *et al.*, 1987; Brunekreef *et al.*, 1983; Lepow *et al.*, 1975), smelter (Roels *et al.*, 1980) and mining (Bornschein *et al.*, 1989; Gallacher *et al.*, 1984a) sites as a direct function of hand-lead concentration. Secondly, there is an inverse relationship of soil/dust particle size to the amount of material adhering to hands (Duggan *et al.*, 1985; Que Hee *et al.*, 1985). Lead-bearing particles of < 100 mesh (<150 μm) not only adhere most tightly to children's hands (Bornschein *et al.*, 1987; Duggan *et al.*, 1985; Que Hee *et al.*, 1985), but are readily mobilized in gastric or other acidic media (Healy *et al.*, 1982; Day *et al.*, 1979; Harrison, 1979). Finally, the smaller the soil/dust particle, the higher the relative concentration of lead and other elements (*e.g.* Van Borm *et al.*, 1988; Spittler and Feder, 1979).

The lead-containing matrix and lead bioavailability

Matrix effects on lead bioavailability, in the form of interactions of lead with various nutrients in the diet, have been described in an earlier section. The impact of lead-containing non-food media of a geochemical or formulary origin, *e.g.* geochemically diverse soils, gangue matrix in mill tailings or crushed ore (*e.g.* silicate, barite), polymerized oil film in leaded paint, on gastrointestinal bioavailability has not been extensively studied as a separate factor.

This is particularly the case for lead-contaminated soils, dusts and such geochemically related media as metalliferous ore particles and mill tailings. Available data make it clear that the level of physical and chemical heterogeneity within and among these media is considerable, and this factor would be reflected in lead bioavailability. Part of these differences are attributable to the already discussed parameters of chemical speciation and particle size. Matrix effects on *in vivo* lead bioavailability take on increasing importance as the toxicity threshold for risk populations continues to be revised downward. With current concerns about Pb–B levels starting at a blood level of 0.5 μmol L^{-1} (10 μg dL^{-1}) (Mushak *et al.*, 1989; US EPA, 1989, 1986), even those media from which lead is only moderately bioavailable now take on significance.

Few controlled clinical or experimental animal studies of medium matrix effects on lead bioavailability have appeared (refer, however, to several animal studies described in these

Proceedings [illegible] environmental epidemiology, occupational exposur biota data to indirectly assess lead bioavailabilit commonly done by analysing relationships of ex toxicity biomarkers to lead levels in various source media. Table 6 sets forth illustrative results with huma exposed to dust and soil lead contaminated by such paint and atmospheric fallout. It must be remembered studies of environmental exposures as those in Table an integrated measure in blood of bioavailability from dominant sources of exposure. Bioavailability assess way is commonly compared to other surveys and usual be fractionally apportioned to each of the specific present, *e.g.* leaded gasoline combustion, lead weathering, point source emissions, without app statistical, environmental or other analyses.

Soil and/or dust lead arising from paint weat chalking (Bornschein *et al.*, 1987; Clark *et al.*, 1987 and Harrison, 1985; Charney *et al.*, 1983; Stark *et* and atmospheric fallout from mobile sources (leaded (Lyngbye *et al.*, 1988; Brunekreef, 1984; Rabinow 1984; Brunekreef *et al.*, 1983) or point sources (smelt CDC, 1986; Angle *et al.*, 1984; Yankel *et al.*, 19[illegible] widely associated with significant contributions to t dentine; Lyngbye *et al.*, 1988), especially when exami regard to blood-lead elevation rates per unit increase lead.

Quantitative studies of lead source apportion household dust and child hand lead indicate that inter lead is a significant contributor to Pb–B in children re old housing of older urban areas, particularly housing of deterioration (Bornschein *et al.*, 1987; Clark *et a* US EPA, 1986; Farfel, 1985; US CDC, 198 well-established bioavailability of lead from paint amplified by the persistence of such dust even with lead abatement. In a number of studies, failure to remove associated with abatement either limits the full redu Pb–B levels (Charney *et al.*, 1983) or may even lead t higher exposure (Amitai *et al.*, 1987; Rey-Alvarez *et al*

As can be seen in Table 6, urban and smelter produce a wide range of blood-lead increments pe mg PB kg^{-1} soil/dust. The US EPA (1989) has estim average slope for point sources, *i.e.* change in blood l 1,000 mg Pb kg^{-1} medium, as being somewhat abo μmol L^{-1} (2 μg dL^{-1}) per 1,000 mg kg^{-1}, but slopes for sites cover a very broad range. The high end of the slop can be assumed to reflect some complex mix o bioavailable lead in media and higher host vulnerabil EPA, 1986, 1989).

Transportable workplace lead and then contamin these workers' homes where preschool children res produce both elevated body-lead burdens and toxicity and Mushak, 1982; Dolcourt *et al.*, 1978; Baker *et al.* Milar and Mushak (1982) and Baker *et al.* (1977) no blood lead begins to be affected at exposure levels o mg kg^{-1} dust using a Pb–B level of 2 μmol L^{-1} (40 μ as threshold. The present level of concern of 0.5–0.75 μ (10–15 μg dL^{-1}) (Mushak *et al.*, 1989; ATSDR, 1988; U 1986) would presumably show a more robust respon lead-bearing medium at issue is highly enriched in le such lead is relatively quite bioavailable (*e.g.* the oxide

Table 6 *Selected epidemiological studies of dust and soil lead impact on children.*

Study group	Study design	Results*	Reference
Leaded paint contributions			
Cincinnati, Ohio inner-city children	Multi-regression analyses of Pb–B *versus* surface dust/soil scrapings with significant paint input	Effect size of 100–1,000 mg kg^{-1} surface scrapings = 0.115 μmol L^{-1} per 1,000 mg Pb kg^{-1}	Bornschein *et al.*, 1987 Clark *et al.*, 1987
New Haven, Ct inner-city children in 3 age bands: 0–1, 2–3, 4–7 years	Pb in house dust at differing levels with leaded paint as a variable	Children 0–1 years old showed a slope of 0.2 μmol L^{-1} per 1,000 mg Pb kg^{-1}	Stark *et al.*, 1982
High-risk Baltimore, MD, children 15–72 months-old w/elevated Pb (n = 14) *vs* controls (n = 35)	Dust Pb in test homes abated by cleaning team and Pb–B monitored	Pb–B of children with dust Pb removal decreased 0.35 μmol L^{-1}; dust returned to old levels quickly. No correlation Pb–B *vs* dust Pb	Charney *et al.*, 1983
British environmental sample study	Quantification of paint Pb input to street and household dusts; paints had moderate Pb	Paint Pb in street dusts up to 20%, and up to 15% in house dust; higher paint Pb would have higher % input	Sturges and Harrison, 1985
Leaded gasoline/fallout			
Nursery school children 4–6 years old (n = 195) in city and suburbs	Pb–B *vs* air Pb relationship integrating Pb fallout from mainly auto emissions in air	An adjusted slope of 0.425 μmol L^{-1} per μg Pb m^{-3}	Brunekreef *et al.*, 1983 Brunekreef, 1984
Urban Danish children (total n = 1302)	Case-referent study of Pb in shed teeth *vs* traffic density and ages *vs* traffic Pb exposure	Pb–teeth were significantly, positively correlated with traffic density at ages 0.5–2 years	Lyngbye *et al.*, 1988
Mainly middle-class Boston infants studied longitudinally (n = 249)	Environmental and Pb–B levels measured up to 24 months age Dust/soil Pb would reflect traffic density by fallout	Pb–air and Pb–B highly correlated, slope = 0.45 μmol L^{-1} per μg m^{-3}	Rabinowitz *et al.*, 1984
Smelter sites			
Children living varying distances from closed smelter in Idaho	Analysis of dust/soil Pb and Pb–B *vs* distance from smelter for relationships	Differences in Pb–B of 0.45 μmol L^{-1} for dust difference of ~2,800 mg kg^{-1} and soil ~ 3,000 mg kg^{-1}	CDC, 1986
Omaha inner-city children near primary and secondary Pb smelter	Statistical analyses for direct plus indirect (soil/dust) Pb from emissions in 1,075 samples	Slopes: Air: 0.1 μmol L^{-1} μg^{-1} m^{-3} Soil: 0.34 μmol L^{-1} per 1,000 mg kg^{-1} Dust: 0.36 μmol L^{-1} per 1,000 mg kg^{-1}	Angle *et al.*, 1984
Operating smelter community in Idaho children 1–9 years old stratified by distance (n = 919)	Multi-regression analyses of air, dust and soil Pb *vs* Pb–B	Soil: 0.055 μmol L^{-1} per 1,000 mg kg^{-1} Dust: 0.01 μmol L^{-1} per 1,000 mg kg^{-1}	Yankel *et al.*, 1977

* 1 μmol L^{-1} Pb–B = 20 μg dL^{-1}.

Table 7. Studies of lead bioavailability in areas with mining-related wastes

Study group	Study design	Results*	Reference
Children			
English children in mining area (Derbyshire) or control site (total n = 82)	Pb–B and Pb–soil stratified by three levels. No control for other sources. QA/QC unknown	Slope = 0.032 μmol L^{-1} per 1,000 mg kg^{-1}	Barltrop, 1975
Australian children in mining town w/ mill tailings *vs* control town (total n = 181)	Analysis of relationship of Pb–B in tailings town *vs* control site: 75% of children >7 years old; 25% 5–7 years old	Statistically significant differences in Pb–Bs in two towns	Heyworth *et al.*, 198
Children 1–3 years old (n = 61) and mothers (n = 58) in Welsh mining area *vs* control towns	Analysis of Pb–B *vs* hand Pb (pica) in children; Pb–B *vs* vegetable Pb in mothers	Children's hand Pb was important contributor to Pb–B. Mining area Pb–B > controls ($p < 0.05$). Mother's Pb–B in mining area > controls ($p < 0.0001$)	Gallacher, 1984a,b
Children <72 months in former mining town in Colorado (n = 150; 63% total)	Multi-regression of Pb–B *vs* sources. Pb–B distribution also reported	Arithmetic/geometric Pb–B mean = 0.51/0.44 μmol L^{-1} Pb–B/soil Pb slope = 0.24 μmol L^{-1} per 1,000 mg kg^{-1} Pb–B values increased at soil Pb > 500 mg kg^{-1}. Pb–B > 0.5 μmol L^{-1} = 41% Pb–B > 0.75 μmol L^{-1} = 15%	Colorado Departmen Health/US ATSDR,
Children ≤ 72 months in another former mining town in Colorado Colorado (n = 94) *vs* controls	Multi-regression of Pb–B *vs* environmental Pb sources. Pb–B *vs* Pb–soil in 18 month-old children	Arithmetic mean 0.3 μmol L^{-1} Effect size (for range of 100 to 1,000 mg kg^{-1} soil) 0.185 μmol L^{-1} per 1,000 mg Pb kg^{-1}; Pb–B correlated w/ hand Pb up to 24 months old	Bornschein *et al.*, 19
Children in Alaskan community with lead ore terminal	Pb–B survey of children, older residents, 1988 and 1989	1989 survey: 23% Pb–B > 0.5 μmol L^{-1} for 0–18 year-olds. No analysis of Pb–B *vs* media Pb	Maddaugh, 1989
Mill and mine workers			
Ore mill workers in Missouri lead belt (n = 15)	Pb–B and Pb–urine *vs* Pb–total air or Pb–respirable air	No significant correlation of Pb–B with respirable or total Pb–air except for non-smokers: mean respirable air *vs* Pb–B (r = 0.94, p = 0.01)	Roy *et al.*, 1977
Lead miners (n = 89), flotation mill workers (n = 19), grinding/ bagging workers (n = 8)	Mean Pb–B levels for three worker categories	Mean Pb–B of miners = 1.0 μmol L^{-1}; mill workers = 2.75 μmol L^{-1}; grinders/baggers (Feb 1982 survey) = 6.1 μmol L^{-1} (May 1982 survey after clean-up) = 3.55 μmol L^{-1}	Dornan *et al.*, 1986
Ecological biota			
Pet dogs (n = 129) grouped by location	Statistical comparison of mean Pb–B level for dogs in mining, smelter, urban and rural sites	Pb–Bs of mining site dogs significantly higher than those in other groups; 15% of these had Pb–B > 1.75 μmol L^{-1}	Koh and Babidge, 198
Longear sun fish (*Lepomis megalotis*)	Pb–B and toxicity measured from tailing contaminated river vs. control site	Pb–B elevated; depressed δ–ALA–D activity; bone and collagen impairment	Dwyer *et al.*, 1988
Suckers (Pisces: *Catostomidae*)	Pb–B and hematotoxic indices in tailing-impacted *vs* control rivers	Elevated Pb–B, depressed δ–ALA–D activity	Schmitt *et al.*, 1984
Riparian wildlife, 5 species: bullfrogs, muskrats, green-backed herons, water snakes, swallows	Comparative tissue Pb levels, downstream *vs* upstream areas in tailing-contaminated rivers	4 of 5 species had significant elevations of Pb in tissues due to tailings impact	Niethammer *et al.*, 19

* 1 μmol L^{-1} Pb–B = 20 μg dL^{-1}.

Studies of mining sites and associated wastes have been sporadic and have generally been limited in statistical design and quality assurance/quality control, but they indicate that lead in mining waste can be bioavailable, based on statistical association, with the extent of bioavailability varying with composition of these heterogeneous wastes (Table 7). The extent of such bioavailability relative to other dust and soil input sources, however, remains to be fully established in terms of specific physicochemical and geochemical forms and origins.

Such lead sources as weathered mill tailings, unprocessed ore spillage or waste rock overburden are physically and geochemically distinct media, and would be expected to be bioavailable through different mechanisms and to have different bioavailability. Given the recent emergence of these types of sources in the environmental epidemiology of lead, because of continuing downward revisions in the levels of lead exposure deemed acceptable (Mushak *et al.*, 1989; US ATSDR, 1988; US EPA, 1986, 1989), it is useful to attempt to evaluate bioavailability aspects of such lead-containing media (Table 7). Barltrop (1975) compared a lead mining community with a non-mining site in Derbyshire, UK, and reported that there was a modest blood lead rise in the mining area children *versus* controls, *i.e.* an approximate 0.3 μmol L^{-1} (6 μg dL^{-1}) rise in Pb–B when mean soil lead differed by 10,000 mg kg^{-1} (Table 7). This study provided no control for lead intakes from other media for both sites and did not utilize any apparent QA/QC protocol. Plus, the high calcium content of Derbyshire soils limits applicability of results to other site soils.

Heyworth *et al.* (1981) reported that an Australian town with widely dispersed lead-mill tailings showed statistically significant higher Pb–B levels in the town's children compared to a reference town without mill tailings. The significant difference was seen despite the fact that three-quarters of the tailing town children were over seven years of age; younger children in the 2–4 years age range who ingest larger amounts of dust and soil would be expected to show an even more robust response.

Several reports by Gallacher *et al.* (1984a, 1984b) indicated that lead exposure to mining waste in a Welsh mining area, compared with a control site, is associated with sufficient bioavailability of the toxicant to elevate blood-lead levels, either by direct contact by children from 1 to 3 years old with leaded material on their hands (Gallacher *et al.*, 1984a) or via lead transfer to garden crops and subsequent consumption by women in the mining community (Gallacher *et al.*, 1984b).

A detailed epidemiological study of a Colorado (USA) mining town heavily impacted for more than 100 years by smelter, mill and mine waste was recently reported, with data on children's blood- lead levels and their sources (Colorado Department of Health, 1990). The survey centred on young children and included measurement of blood-lead levels and inferential statistical analysis (stepwise forward regression) of blood lead–environmental media relationships. Most of the town's children <72 months old (63%) participated. The arithmetic and geometric mean Pb–B levels were 0.50 μmol L^{-1} (10.1 μg dL^{-1}) and 0.44 μmol L^{-1} (8.7 μg dL^{-1}) respectively. Children with Pb–B levels >0.50 μmol L^{-1} (10.1 μg dL^{-1}), a current level of concern, comprised 41% of the sample; levels >0.75 μmol L^{-1} (15 μg dL^{-1}) constituted 15% of these children/ Pb–B levels had a geometric standard deviation of 1.79, most likely reflecting an epicentric ('hot spot') mix of exposure sources. The strongest statistical association was found between child Pb–B and soil core samples with odds ratios showing that soil Pb >500 mg kg^{-1} produces elevated Pb–B in these children. A slope of 0.24 μmol L^{-1} (4.8 μg dL^{-1}) per 1,000 mg Pb kg^{-1} soil, over the range of 100–1,000 mg Pb kg^{-1} soil, was calculated.

Bornschein and co-workers (1989) examined the relationship of blood lead in children in another former lead mining town in Colorado, and found that young children were exposed (via the hand-lead pathway in those of 24 months old or younger) to leaded dust and soil-surface lead sufficient to elevate child Pb–B, in a relationship of 0.1–0.2 μmol L^{-1} (2–4 μg dL^{-1}) Pb–B per 1,000 mg Pb kg^{-1} in the soil/surface medium. This study does not permit precise identification of the type of mining waste at issue, *e.g.* weathered mill tailings, ore spillage or weathered waste rock, but the inverse relationship of blood lead with distance from the railroad line and the flood line of the local river, as well as no relationship to distance from the tailings site, suggests that the source of lead exposure is more apt to be cumulative loss of rail-borne ore rather than mill tailings.

Two surveys of blood lead of children and older residents in an Alaskan community with an ore-loading terminal made in 1988 and 1989 (Middaugh *et al.*, 1989) do not permit conclusions (Table 7) as to whether blood lead in very young children can be elevated by lead ore exposure. The child sample size was small and no statistical analyses of Pb–B *versus* lead in ore or other media were done. The percent of subjects 0–18 years old with Pb–B over 0.5 μmol L^{-1} (10 μg dL^{-1}), (range 0.55–0.66 μmol L^{-1}) in 1989 was found to be 21%. Freshly-mined ore with a significant number of large particles and a relatively more intact gangue matrix may not be comparable in lead bioavailability to other mining-related wastes, *e.g.*, weathered mill tailings (see below).

Steel *et al.* (1990) have attempted to help define the level of bioavailability of lead in mining-related material by including an analysis of the relationship of ore-mill lead, presumably mainly geochemical lead sulphide, to worker blood-lead levels. Such comparisons are highly limited in value for exposures of general populations to historical mine waste since: (1) the principal focus for health risk assessment in leaded mine waste exposures are very young children and pregnant women with a range of vulnerabilities and exposure rates, not adult workers who absorb much less lead compared to children, and who exhibit the well-known 'healthy worker' effect, and (2) workers are exposed to freshly-generated particles or ore and tailings rather than the weathered and more bioavailable material of, say, old tailing piles.

Nonetheless, several workplace studies have attempted to examine mill tailing and related extractive process forms in terms of worker blood-lead levels. These studies vary as to design quality and worker sample size. Roy *et al.* (1977) surveyed 15 ore mill workers for complete study for the existence of air lead–blood lead relationships and found a poor correlation of respirable or total air Pb *versus* Pb–B across the group, *i.e.* no apparent blood lead–air lead slope. The main exception to these findings was the relationship of respirable air to Pb–B of non-smokers.

This is not surprising, given the generally poor relationship for air lead *versus* Pb–B found by the large studies of many workers by Garside *et al.* (1982) and Bishop and Hill

[illegible] These surveys both showed that little of the variance in Pb–B is explained by workplace air lead. The studies of Bishop and Hill (1983) and Gartside *et al.* (1982) are supported by the epidemiological studies of Chavalitnikikul *et al.* (1984) who documented an association of workplace surface dust lead, facial lead and hand lead with Pb–B levels in battery workers. In a later study, Dorman (1986) reported group mean Pb–B results for three work categories associated with lead ore mining and processing: lead miners, mill workers using froth flotation, and grinding/bagging employees. As noted in Table 7, the miners showed hardly any elevation in Pb–B, while there were significant mean Pb–B elevations for 19 flotation workers and for 8 dry-grinding and bagging employees (Table 7).

Bioavailability of lead in mining waste sufficient to elevate blood lead has also been documented in terrestrial and aquatic biota (Table 7). Koh and Babidge (1986) reported that domesticated dogs ($n = 129$) in the lead mining community of Broken Hill, Australia, had significantly higher mean Pb–B levels than groups of dogs from any of three other sites, including one having a lead smelter; 15% of the dogs had a Pb–B of 1.75 μmol L^{-1} (35 μg dL^{-1}) or higher.

In the longear sunfish (*Lepomis megalotis*; Dwyer *et al.*, 1988) and species of suckers (Pisces: *Catostomidae*; Schmitt *et al.*, 1984) exposed to leaded mill tailings entering the Big River of Missouri's 'Old Lead Belt', it was found that blood lead was significantly elevated, and there was marked inhibition of δ-aminolevulinic acid dehydratase (δ-ALA-D) activity. There were also marked adverse changes in collagen and bone of fish (Dwyer *et al.*, 1988) exposed to lead and other toxic elements. Likewise, four of five species of riparian vertebrates along two rivers in the Missouri lead mining region were found to have higher Pb burdens than those biota from a reference site (Niethammer *et al.*, 1985).

Of direct relevance to the human and ecological lead bioavailability studies are several reports describing such parameters of mill-tailing lead as solubility, chemical form speciation and particle size. Mill tailing leachability data of Harwood (1984) showed that 55–69% of lead in these tailings were bound as oxide, sulphate or carbonate, depending on extraction medium. The sulphide amounted to only 7% of all chemical species present.

A detailed study of mill tailings was recently carried out at a Superfund site in Utah (Montgomery Engineering, 1989) and included particle-size distribution and toxic metal content studies. Study results, gathered under the rigorous QA/QC requirements of the US Environmental Protection Agency's Superfund site evaluation protocols, showed that about 50% of lead in lead ore mill tailings was extractable by ammonium acetate solution (*i.e.* was present in oxidised, *i.e.* non-sulphide forms). Tailing particle size distribution analysis for composite surface plus core samples showed over 60% of particles were of smaller diameter than 100-mesh and about 25% of particles were 10 μm or less in size. It was also found, consistent with the results of van Borm *et al.* (1988) and Spittler and Feder (1979), described earlier, that the majority of total mass of lead and other toxic elements were to be found on the smallest particles of tailings.

A second investigation of the Utah site is that of Drexler (1990 contract report; article in preparation) who carried out microprobe geochemical structural analysis of tailings, smelter slag and contaminated residential soils proximate to the tailing site. Chemical speciation studies of the tailings and [illegible] contaminated soils showed that lead was present in considerable number of chemical forms, with lead sulphide often being the minor species. In addition, tailing particles contaminating particles in residential soils were often to be less than 100–150 μm in size.

Overview of biophysico-chemical factors in GI lead-uptake

All lead that enters the human GI tract exists in chemical/geochemical form, is often present in particulate material of highly variable size (diameter) and is enclosed in some matrix which variably interacts with the biochemical milieu of the GI tract, particularly basal and induced gastric acid.

Many forms of lead are rendered bioavailable in the human GI tract, and the behaviour of various chemical forms of lead *in vivo* is not well mimicked by such simple in vitro tests as solubility. For example, lead sulphide which is ingested in precise dose or inadvertently by populations using [illegible] cosmetics is absorbed extensively depending on particle size and is also associated with documented toxicity.

Lead bioavailability in the human GI tract is also affected by particle size, particularly for diameters of 250 μm or less, based on epidemiological and experimental data showing enhanced bioavailability in smaller sizes, which becomes significant at a theoretically determinable small particle size. This is supported by the known higher retention of dust lead than food lead in children for particles below 100 μm.

The chemical/geochemical matrix in which lead is ingested is found can be variably transformed in the GI tract with respect to release of bioavailable lead. A major mechanism of lead transformation is to be found in the stomach, with the action of both basal and induced gastric juice. The lead-containing matrix of ingested lead is quite diverse in composition and this determines the relative ease of lead release. While the particular chemical form and the particle size of the lead-containing material are known determinants of reactivity, the matrix composition is also important.

The biochemical matrix of human diets has a major influence on lead absorption, operating principally through nutrient–lead interactions discussed in this article.

Non-dietary matrices, such as leaded paints, lead-bearing dusts and contaminated soils, are associated with a range of bioavailability. Potential or documented bioavailability of lead in dusts associated with ambient fallout, paint, re-entrained soil deposition and such industrial process waste as ore tailings have been documented. Not only do there are gradations of bioavailability within these matrices. In mineralogical media, the available evidence collectively suggests that lead in weathered mill tailings would be more bioavailable than lead in freshly mined ore, which in turn may be more bioavailable than the element in weathered overburden mine rock.

As the tolerable levels of lead body burden in human populations, especially preschool children, continue to be revised downward, sources of lead which were not given much attention in the past increase in importance as inputs to exposure markers such as blood lead. This includes the potential impact of mining waste on human populations. Such wastes are highly heterogeneous in nature and this would be reflected in the bioavailability of lead. Available epidemiologic

geophysical-chemical studies document this and suggest that there is lead exposure potential in weathering tailings and perhaps other waste forms relative to a new level of concern of 0.5 μmol $^{-1}$ (10 μg dL^{-1}) for blood lead.

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Bioavailability of Lead in Mining Wastes: An Oral Intubation Study in Young Swine

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Introduction

The incidental ingestion of soil as a result of hand-to-mouth and object-to-mouth behaviors is recognized as a significant source of exposure of young children to toxicants present in soil and household dust (Calabrese *et al.*, 1987). In particular, it is generally accepted that these exposure pathways may be the most important contributors to non-dietary lead exposures (Barltrop, 1973; USEPA, 1989). Thus, where there is significant contamination of residential soils, a crucial determining factor for systematic exposure is the availability of soil/dust lead for absorption from the gastrointestinal (GI) tract. Recently, the bioavailability of ingested lead has become a significant issue in establishing clean-up levels for soils contaminated with wastes from mining and/or milling operations. Two hypotheses have been put forward which suggest that lead from mining/milling activities may be less bioavailable than that from other lead sources such as smelter emissions and lead paint dust (see Steele *et al.*, 1989). Basically, these arguments are (1) lead at many mining sites may occur as lead sulfide (PbS) which is relatively insoluble in water at neutral pH compared to other common lead containing compounds, and, thus, may pass through the GI tract without appreciable dissolution, and (2) lead in soils at mining sites may exist as particles which are relatively large, and are thus both less likely to be ingested and to dissolve in GI fluids. However, the basis for these assumptions lacks an empirical foundation. For example, there is little published data on the forms of lead that occur in soils near smelter, milling or mining sites. Similarly, little data exist on the distribution of lead in different particle size fractions at either smelter sites or mining/milling sites.

In order to further elucidate the bioavailability of lead from mining/milling wastes, EPA Region VIII initiated a study in collaboration with Michigan State University of GI uptake of lead in mill tailings taken from Midvale, UT. The lead present in deposits adjacent to the community of Midvale is derived primarily from galena ore and thus should consist mostly of lead as lead sulfide crystals. Further, because past milling processes often produced wastes with relatively large grain size (Benedict, 1955), most of the lead was predicted to be associated with relatively large (greater than about 100 µm) soil particles. Particles larger than 100 µm probably will not adhere efficiently to skin and thus will not be available for transfer to the mouth during typical hand-to-mouth behaviors (Que Hee et al., 1985). Thus, based on the above arguments, lead in the Midvale tailings should be relatively unavailable for absorption from the GI tract, compared with absorption of a water soluble lead salt such as lead nitrate. In fact, one would predict that availability would be similar to that of reagent grade lead sulfide, providing that tailings lead was not 'buried' in a silicate or pyrite matrix which could further reduce bioavailability. The EPA/MSU study was designed to test the following null hypothesis: (1) that lead in the mine tailings is unavailable for absorption from the gut of pigs and (2) that absorption of lead in tailings is not different than that of lead sulfide and lead nitrate.

Materials and Methods

Animal model

Because lead intoxification is a matter of concern primarily for young children (age 6 months to 6 years, EPA 1989), an animal model chosen for research on bioavailability should reflect as much as possible the behavior, and GI physiology and biochemistry of young children. As discussed in detail in another report in this symposium (Weis and LaVelle, 1991), rodent and lagomorph models seemed not to meet the above criteria and so were rejected as candidate models for the study. Several other potential models were investigated, and the one which seemed to most clearly meet study criteria was the recently weaned pig (Weis and LaVelle, 1991). Young pigs have been used extensively as a model for children's GI function (Dodds, 1982; Miller and Ullrey, 1987; Weis and LaVelle, 1991). Moreover, physiology and biochemistry of

Table 1 *Doses of lead for mixtures of control soil and lead from different sources*

	Dose group				
	Low tailings	Medium tailings	High tailings	PbS	$PbNO_3$
Nominal lead dose	0.44	0.88	1.76	1.76	1.76
Measured lead dose	0.56	1.05	1.84	1.52	1.67

All values are mg Pb/kg body weight.

calcium and, by extension, lead metabolism, appear to be similar in young pigs and children (Weis and LaVelle, 1991).

Weaned, male, cross-bred swine (*Sus scrofa*) used for the study were selected according to age (45 to 47 days) from the nursery area of the Michigan State University swine facility. Animals were allowed to acclimate in experimental cages for 5 to 10 days. Animals were fed 4 % of body weight per day, an amount which met or exceeded all nutrient requirements for this age of swine set by the Committee on Animal Nutrition of the National Research Council. Animals were fed twice daily and water was provided by mixing equal volumes with the food to make a slurry. This minimized food spillage by the pigs. Additional water was provided at midday.

Lead sources

Midvale, UT, a community of about 30,000 located 12 miles south of Salt Lake City, is the site of past milling and smelting activities. The milling operation was active from 1910 to 1970. It produced about 14,000,000 cubic yards of mine tailings from the processing of lead, copper and zinc ores. The tailings pile now covers over 260 acres and, in places, is over 50 feet deep.

Lead from tailings was obtained from an archived grab sample taken from the surface of the tailings deposit. The surface sample was deemed appropriate since it is surface material which is transported *via* wind and which children may contact when playing on contaminated soil. The tailings sample was screened through a 100-mesh sieve to obtain a fraction of particles smaller than about 150 µm, close to the size fraction expected to adhere to human skin. Analysis of the material before and after sieving indicated that lead concentration in the whole tailings sample (16,900 ppm, USEPA, 1990) was similar to that in the sieved fraction (17,200 ppm, Billing, 1990).

Reagent grade lead nitrate and lead sulfide were used as positive controls and were obtained from Fluka Chemicka-Biochemica, 980 S 2nd Street, Nonkonkoma, NY 11779 and Sigma Chemical Co, PO Box 14508, St Louis, MO 63178, respectively.

Control soil was obtained from a surface grab sample taken in an area of Midvale, UT where lead contamination was expected to be minimal. This soil was also passed through a 100 mesh sieve. Analysis of the sieved fraction of the control soil indicated a lead concentration of 150 ppm.

To obtain different doses of lead, control soil was mixed with different proportions of the sieved tailings or the r grade lead salts. Doses were mixed such that the amount to be given to each animal on a mg per kg basis was cor in 292 mg of soil mixture. Knowing the concentrations in the control soil and mine tailings and the d concentration of lead in the final mixture, a Pearson Squa used to calculate the ratio of control soil to tailings requ similar approach was used with the positive controls an in that case, the lead concentration was calculated fr formula weight. Appropriate aliquants of mixtures weighed on a top-loading gram scale and mixed thorou manual shaking for at least 5 minutes in acid-c polyethylene containers.

Actual lead concentrations in the tailings samp control soil and the mixtures were determined by three di methods, X-ray fluorescence, and atomic absorption fol nitric or hydrofluoric digestions.

Dosing protocol

Animals were assigned randomly to one of five tre groups, three animals per group, for each of two id experimental blocks completed sequentially. Animals group were administered a single dose of one of the abov mixes, 292 mg soil mix per kg body weight, as a slurry mL of distilled water, by intubation. The mixing vessel a stomach tube were then rinsed with an additional 20 distilled water to ensure complete delivery of the dose. A were watched closely for emesis for the first hour after c After 120 hours, the same dose was readministered to ea using the same procedures. Thus, each animal was giv same dose twice, as a check on intra-animal variability.

Three groups of animals received mixtures of tailin control soil. In addition, one group of animals receive sulfide mixed with control soil and the final group receiv nitrate mixed with control soil. Nominal and measure doses for each group are provided in Table 1. Pilot indicated that background lead concentrations in the bl pigs were very low (below the quantification limit of 40 µ and apparently stable over time, and that administrat control soil alone did not cause a measurable incre background blood lead concentrations after a single dose in this study, each animal served as its own control, u blood lead measurements serving to establish the basal lead level.

Table 2 *Methods for atomic absorption spectrophotometry*

Wavelength	283.4 nm
Slit width	1.4 nm
Conditions	Dry - 60 s, 35!135 (C ramp Ashing - 30 s, 600 (C Atomization - 7 s, 2,000 (C
Matrix Modifier	Triton X-100, 0.5 % wt/v Nitric Acid, 0.2 % v/v Ammonium phosphate dibasic, 0.2 % wt/v

Blood sampling and analysis (see Tables 2 and 3)

Immediately before administering the soil mixes, and at 1, 2, 4, 6, 8, 12, 24, 48, 72, and 96 hours post dosing, blood samples were taken from the jugular vein with a closed Vacutainer system (Becton-Dickinson Vacutainer Systems, Rutherford, NJ 07070). Samples were taken initially in tubes containing EDTA as an anticoagulant and stored at 4° C. As soon as possible after collection, samples were split into three 1 mL aliquots. One tube was stored at 4° C for future use, a second was analyzed by AA (see below) and the third was sent to CDC for confirmatory lead analysis.

Whole blood lead concentrations were determined by atomic absorption spectroscopy with an Hitachi model 180-80, Zeeman effect, atomic absorption spectrophotometer equipped with a graphite furnace. Whole blood (100 µL) was mixed with a matrix modifier of triton X-100 and dibasic ammonium phosphate in type II distilled water acidified with ultra pure 16 M nitric acid (Table 2). Blanks, 50, 100, 200 and 300 ppb standards were included in each analytical run.

Results

Interlaboratory blood lead analysis comparisons

The studies were conducted under strict quality assurance procedures. Ninety three percent of the duplicate analyses were within 10 % of one another, with a mean difference of 4.0 %. Ninety six percent of the proficiency standards were within 10 % of the certified values in an interlaboratory comparison (University of Wisconsin).

The results of analyses of blood lead by MSU were plotted against the results obtained on splits of the same samples from CDC (Figure 1). With the exception of one low value obtained by CDC, there was excellent agreement between the two laboratories. The slope of the line is, as predicted, near 1 and the *y* intercept near 0. The close agreement suggests that the blood lead values obtained in the study, even those near the limits of quantification, are accurate.

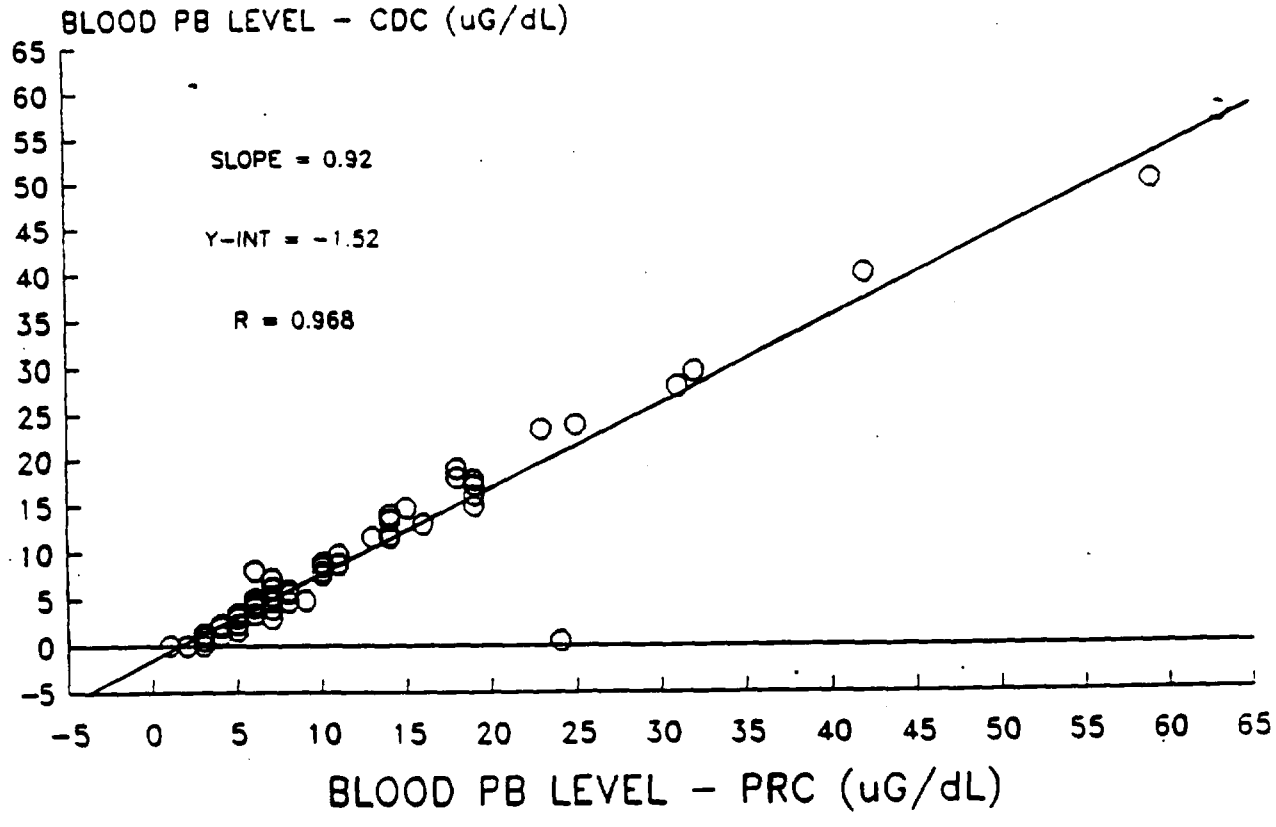

Figure 1 *Comparison of blood Pb analyses run by the Pesticide Research Center (PRC) at Michigan State University with analyses run on split samples by the Centers for disease Control (CDC) in Atlanta. Line is a linear regression from all data points.*

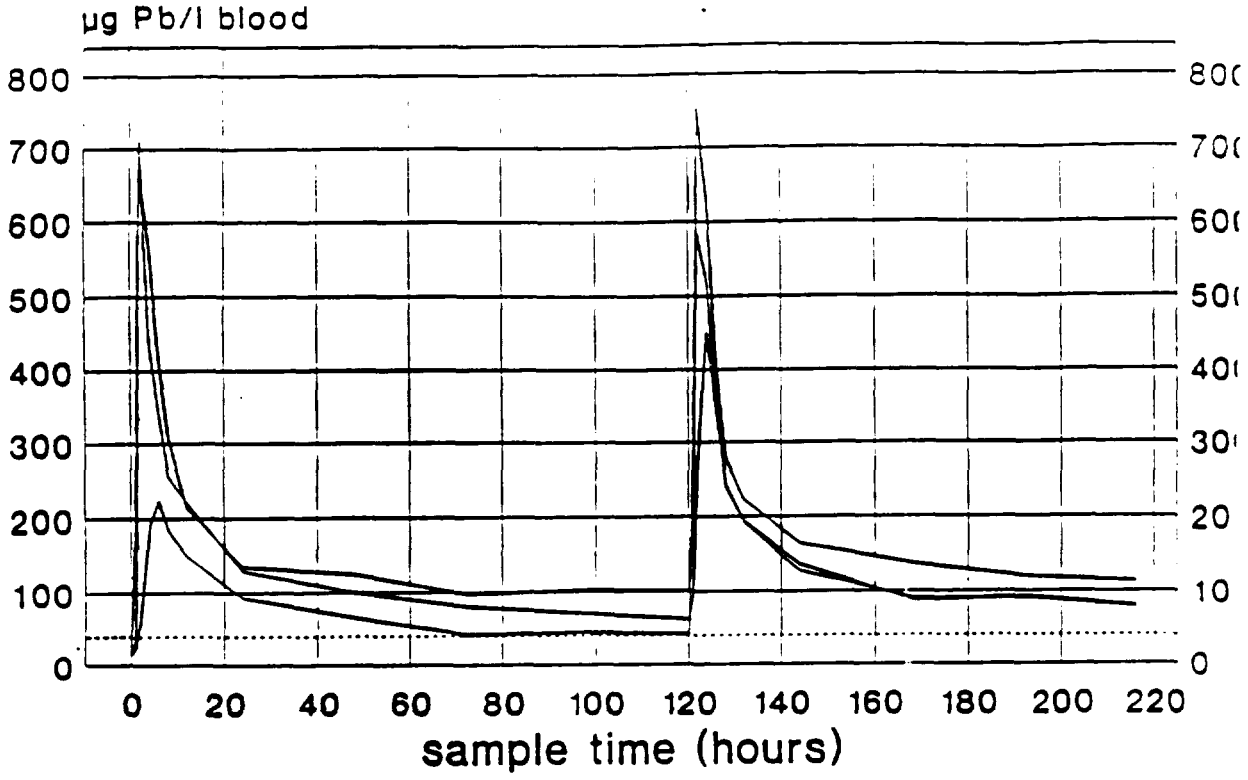

Figure 2 *Representative blood lead/time curves for three pigs given control soil mixed with the greatest amounts of Mi tailings. Dose given to all animals was 1.84 mg Pb/kg body weight. They were dosed by oral introduction at 0 and . dashed line is the quantification limit.*

Blood lead vs time curves

Uptake kinetics of lead were similar among treatments, but variation among individuals was observed (Figure 2). The maximum concentration of lead in blood occurred between 4 and 6 h after dosing, and blood lead levels returned to near background within 96 h. Since relative bioavailability was estimated using area-under-the-curve (AUC) calculations (see below), it is important to note that extrapolation of blood lead curves past 96 hours suggested that contribution to total AUC from 96 to 168 hours (three more days) might have averaged about 8 to 10 %. Thus, estimates of bioavailability should not be greatly influenced by the small amounts of lead which might still be in the blood after 96 hours.

Area under the blood lead/time curves

An approximately linear relationship was observed between dose of lead in tailings and the amount of lead absorbed, as measured by AUC (Figure 3). (AUCs were estimated using Sigma Scan software (Jandel Scientific, Corte Madera, CA 94925) and a digital plotter.) Estimates of AUC for individual blood lead/time curves were combined for all animals (Figures 3 and 4). Lead in tailings at the greatest administered dose was absorbed to a greater extent than was lead nitrate mixed with control soil, although the statistical analysis did not take into account the lower actual dose received by the animals receiving lead nitrate (Figure 4). However, reagent grade lead sulfide mixed with soil was absorbed to a significantly lesser extent ($p < 0.05$). Thus, contrary to the predictions of Steele *et al.* the lead in tailings from the Midvale site more c resembled that of a soluble lead salt ($PbNO_3$) than that less soluble lead sulfide. It is interesting to note, howeve even lead sulfide was absorbed to a measurable extent. B of comparison, absorption of lead in animals administere in tailings at 0.56 mg kg^{-1} was slightly less than that ab by animals given reagent grade lead sulfide at a dose c mg kg^{-1}. Thus, lead in the tailings may be about 2 to 3 more available than reagent grade lead sulfide in this stu

The relative absorption of lead from tailings and fro nitrate is interesting, but may be due, in part, to saturat transport mechanisms in the gut. If the doses of lead f high-dose tailings group and the lead nitrate group wer near those necessary to saturate active transport o estimations of relative bioavailability could be comprom some degree. Thus, it is possible that some difference in r bioavailability between lead nitrate and lead in tailing: have been encountered if both had been administered a doses.

Discussion

The results reported at this symposium are still being a and this paper presents only a partial and preli interpretation of the data. Even so, it seems that interesting conclusions can be reached concerning the bioavailabilities of lead in smelting *vs* mining/milling

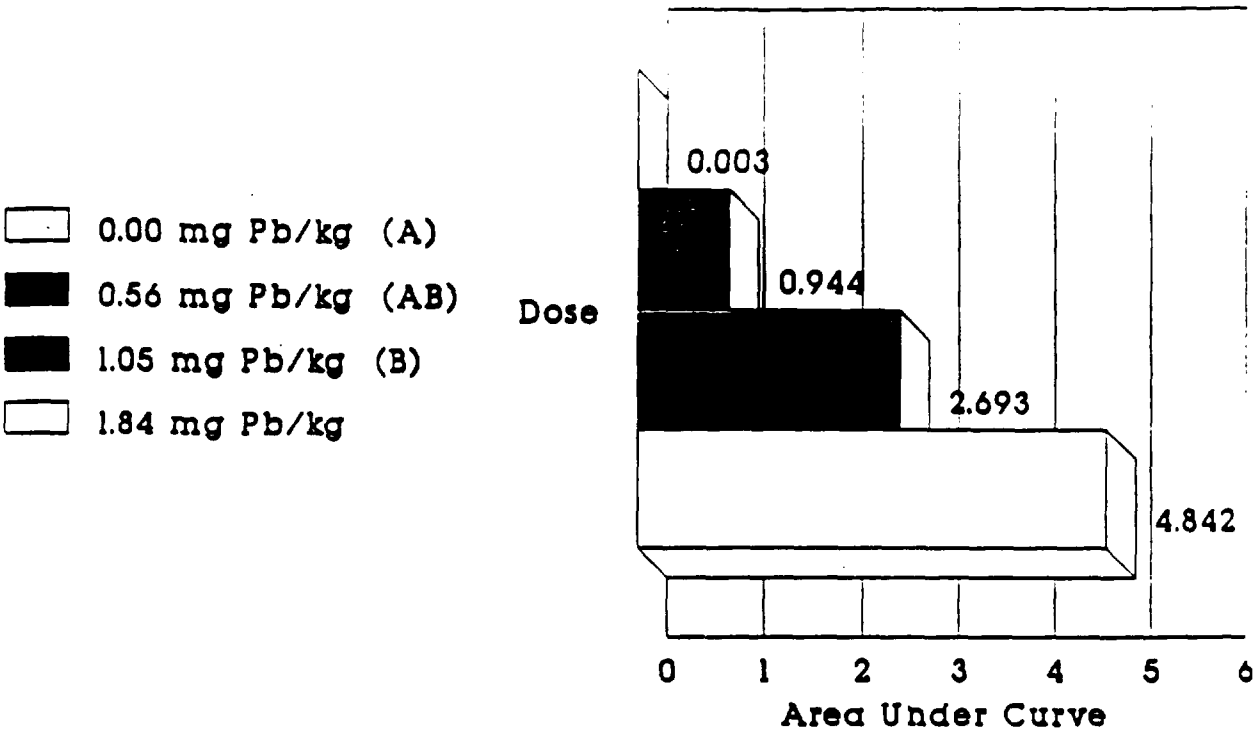

Figure 3 *Average blood lead concentrations for three groups of pigs given control soil mixed with different proportions of tailings from Midvale, UT. The group associated with a dose of 0.00 mg Pb/kg represents the AUC for a hypothetical control group. Since animals which received no dose of lead always had levels of lead in the blood less than the quantitation limit (< 40 µg L^{-1}, this AUC was calculated assuming a blood lead concentration of 40 µg L^{-1}. Means of doses with same letter (A, B) are not significantly different ($p < 0.05$).*

The apparently greater absorption of lead in tailings compared with the lead nitrate control is unexpected. The difference between the two lead forms is partly due to the lesser dose given to the animals receiving lead as lead nitrate. However, other factors may play a role. If the dose of lead in both tailings and lead nitrate were sufficiently high to saturate active lead transport, reversible binding of lead to constituents of stomach and intestinal contents could play a significant role in determining lead absorption. When the amount of lead is sufficiently low that active transport is not saturated, absorption of lead will, in theory, be independent of free lead concentrations, and reversibly bound lead will be fully available for absorption. Active transport will serve to continuously pull the binding equilibrium toward dissociation. Provided that gut transit times are not too short, all bound lead would be available for uptake. At greater lead doses, near or in excess of those that might saturate active processes, bound lead might not be fully available for absorption. Where active transport is saturated, further absorption will depend on the free lead concentration. Bound lead under these conditions may not be completely available. In preparation of material for dosing, control soil was substantially diluted with tailings. The tailings have a low organic content and would be expected to have fewer binding sites for lead than control soil which was taken from the surface of a vegetated area. With fewer binding sites, high doses of lead may lead to a greater free lead concentration in the intestine and, hence, greater lead absorption. When reagent grade lead nitrate was mixed with soil there was little dilution. In this case, increased binding could have led to somewhat decreased absorption.

It is interesting to note that in rats greater than 8 weeks of age, where active transport of calcium (and presumably lead) is absent (Weis and LaVelle, 1991), binding of lead to soil components has been shown to reduce absorption, at least in cases where the amount of soil administered to the pigs in this study (over 2 grams for a 10 kg animal) suggest that similar effects could also have occurred here. Comparison of absorption at lower doses might help determine if binding effects were important in this study.

Regardless of potential differences between availability of lead in tailings and lead nitrate in this study, the results using pigs as an experimental model for lead bioavailability demonstrate that soil in tailings is absorbed by young pigs to a significant extent. Absorption of lead from tailings was significantly greater than that from reagent grade lead sulfide mixed with control soil and appeared to be similar to that of lead nitrate in the control soil mixture. This is consistent with chemical and physical measurements made on the tailings sample. Small particles appeared to contain at least as great a concentration of lead as did the total sample. This suggests that lead is not confined primarily to larger particles at this tailings site. Furthermore, independent electron microprobe analysis of sieved tailings from the Midvale site showed the presence of large numbers of galena crystals with estimated diameters less

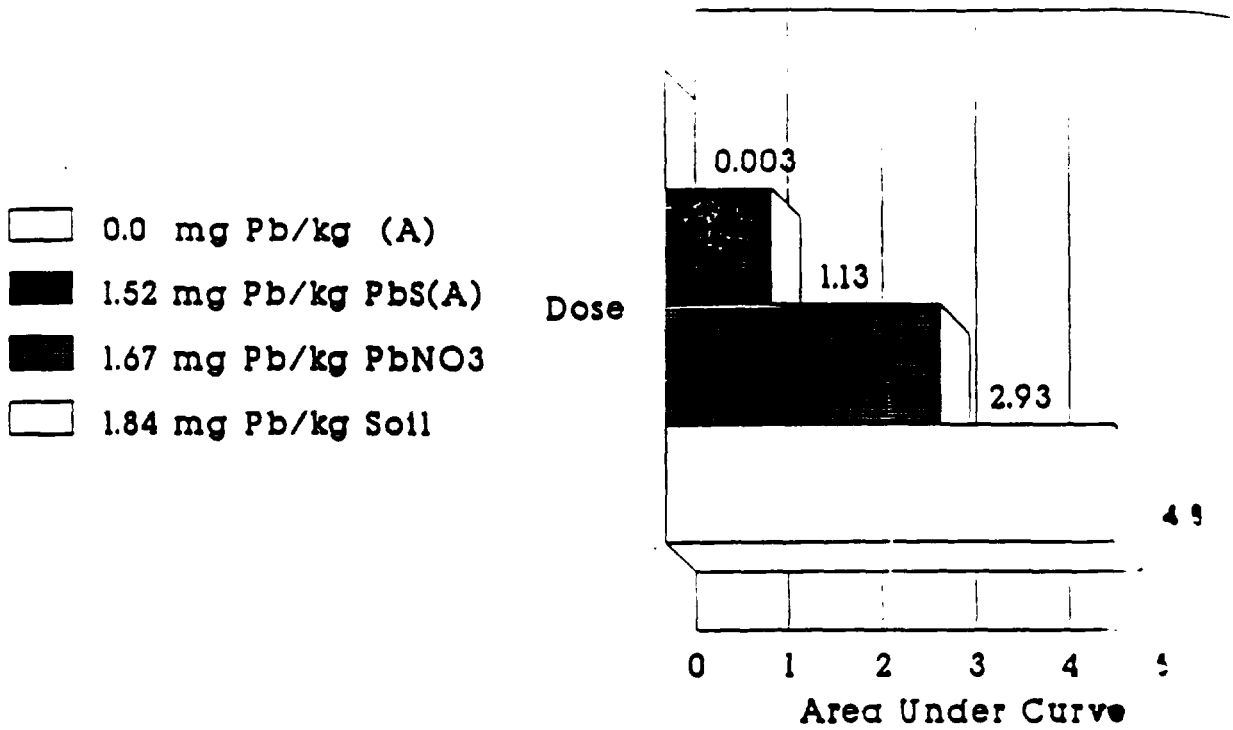

Figure 4 *Average blood lead concentrations for three groups of pigs given control soil mixed with tailings [illegible] reagent grade lead nitrate or reagent grade lead sulfide. The group associated with a dose of 0.00 mg Pb/kg is [illegible] in Figure 3. The statistics were run on the combined data without normalization for differences in dose. Means [illegible] same letter (A/B) are not significantly different ($p < 0.05$).*

than 10 µm (Drexler, personal communication). Particles of this size might be completely dissolved within 50 to 100 minutes in gastric fluids (Healy et al., 1982). In the stomachs of young children, where there would be continued secretion of gastric acids, dissolution could be even more efficient. Finally, the results of the electron microprobe analyses indicate that considerable oxidation of lead in tailings has and is taking place, such that less soluble forms of lead such as PbS are replaced by sulfates and oxides that are considerably more soluble (Drexler 1990, personal communication). Thus, for this milling site, the basic arguments described by Steele et al., 1989 may not hold true. First, much of the lead is present in more soluble forms, which appear to be highly available at, e.g., smelting sites, and second, large amounts of lead are present even in the smallest particles.

The above results are similar to those being collected at other mining/milling sites. For instance, in material from Butte, MT, there seems to be a consistent enrichment of lead and other metals in smaller (100 mesh) particles, a finding opposite of that predicted by the Steele *et al.* analysis for such a mining site. Further, current studies of smelter sites, like East Helena, MT, seem to indicate that considerable contamination may be due to dusts blown from concentrate piles (most of which comes from galena ore deposits). Thus, even at 'pure' smelting sites, such as the smelter facility in East Helena, MT, considerable contamination may come from sources other than stack emissions. The emerging picture seems to indicate that the division between smelting sites on one hand and [illegible] sites on the other may be somewhat artificial. It seems [illegible] that exposures at all sites associated with [illegible] processing of lead-containing ores will be mixed, [illegible] both small particle, lead oxides typical of smelters, and sulfide containing particles and their oxidation products of mining and milling activity. This implies that it may possible to separate smelters from other mining activities basis of bioavailability.

If the above findings in young pigs can be extr young children, lead in mining/milling wastes may pr similar hazard as does lead from other sources. Anat physiological and biochemical similarities between children and the pigs used in this study are presented elsewhere in this volume (Weis and LaVelle, 1991). similarities support the extrapolation of the results to c In addition, the overall pattern of lead uptake from the seems similar in pigs and humans. Based on excretion of Pb-203 in adult volunteers, maximum concentration in blood probably occur before about 6 hours after dosin peak excretion seems to occur at this time or slight (Kehoe, 1961). This is very similar to the timing of pea lead concentrations in young pigs in this study. Assum major differences between adults and young children the shape of the blood lead/time curve, young pigs a model children satisfactorily.

In summary, swine seem to be an appropriate m

young children. Initial results using this model suggest that tailings material from Midvale, UT is more available to young pigs than is reagent grade PbS when presented as a single large dose by intubation. Chemical and physical characterization of the lead in the tailings material suggest that lead is present in small particles, consistent with this relatively high availability. Further, weathering (oxidation) appears to produce lead forms which are more soluble and, thus, potentially more bioavailable. This initial study does not lend support to current arguments that lead from mining/milling activity is significantly less bioavailable than that from other sources and activities.

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Characteristics to Consider when Choosing an Animal Model for the Study of Lead Bioavailability

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Abstract

Most animal studies conducted to determine the bioavailability of lead have, in the past, employed rodents or lagomorphs as experimental models. In this paper issues and data are presented which raise questions and uncertainties about employing rodents or lagomorphs for investigations into the bioavailability of lead. These issues include: (1) the possible role of coprophagy and feeding behavior in reducing estimates of lead bioavailability; (2) anatomical and physiological differences related to coprophagy which may influence estimates of lead bioavailability derived in rats or rabbits; (3) evidence for relatively high biliary excretion of lead by rats and rabbits; (4) the possibility of a strong developmental component to the active transport of lead. The importance of addressing these and other questions in studies designed to determine the bioavailability of lead is discussed.

Introduction

Multimedia exposure of children to lead is recognised as an health problem of international proportions. Ingestion of soil and dust incidental to hand to mouth activity presents one of the principal direct pathways for exposure to non-dietary lead in areas with significant soil contamination. Environmental lead contamination derives from a variety of sources including lead based housepaint, auto emissions, smelter emissions, wind-blown tailings or mine wastes and mine waste deposits which have been used for residential development or have been redistributed as fill material in such areas.

Recently, a debate regarding the relative bioavailability of lead from different sources has developed (Steele *et al.*, 1989). In particular some indirect evidence has been interpreted to suggest that the bioavailability of lead from mining/milling operations is significantly less than that of lead from other sources. A preliminary review of issues pertaining to lead sources and their bioavailability has been presented by Chaney *et al.* (1988). As is evident from this review, a great deal of our present information on lead bioavailability is based on animal studies which used rodents as models. Regardless of the species employed, such studies are most informative if issues pertaining to particle size, metal speciation and chemical matrix are clearly addressed.

In response to the issues raised in the above-cited papers, a study of the site-specific bioavailability of lead in mill tailings has been conducted (LaVelle *et al.*, 1991). It became apparent during the study design phase that many issues relevant to the rat or rabbit models for lead bioavailability had been inadequately addressed in the literature. This paper will present a brief overview of these issues. It is hoped that the information will assist investigators in the design, conduct and interpretation of animal studies on bioavailability of ingested lead. While the material presented has particular importance for [illegible] interested in studies concerning the less soluble species of lead such as might be associated with mining, milling or smelting operations, much of the material presented is applicable to other forms of lead as well.

Definitions of Bioavailability

Definitions of bioavailability via the gastrointestinal tract or other routes may take different forms depending upon the laboratory procedures employed and the experimental design of the investigator. Pharmacological definitions of bioavailability generally consider the area under the blood concentration vs time curve (AUC). Using this method, whole blood concentrations of the xenobiotic in question are plotted vs time following ingestion and are then compared with similar plots following intravenous administration. The ratio of AUC_{ing} to AUC_{iv} times 100 is then taken as a measure of percent absorption of the agent. An understanding of presystemic elimination (*i.e.* net excretion into the alimentary tract) in the animal model employed is important in interpreting estimates of bioavailability using the AUC technique. Thorough study of systemically delivered lead can provide information regarding transepithelial elimination into the alimentary tract. A potential limitation of the AUC technique is that it provides little information regarding non-linearities in the absorption vs time curve over the subchronic or chronic time frame.

Other definitions of bioavailability involve total mass balance where, for example, total chemical excreted in urine and feces and total retained in the body are measured. Such studies are most useful when absorption kinetics are considered. Steady-state blood levels reached after multiple dosing may be used as an indicator of bioavailability. Bioavailability might then be estimated as chemical in urine plus chemical retained in the body divided by the total chemical recovered. Again, knowledge of net excretion into the alimentary tract is essential to accurate estimation of the amount of chemical absorbed.

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Measures of bioavailability using AUC methodology should be distinguished from whole-body uptake of lead or other measures of cumulative body burden. Closely spaced measurements using the AUC methods can provide detailed kinetic information concerning absorption and elimination of lead from the blood. On the other hand, mass balance studies may provide some indication of accumulation of compounds such as lead after repetitive exposures. Coupled with tissue analysis for accumulated lead, mass balance studies augment our understanding of lead distribution. One area requiring further research concerns the kinetics of distribution and mechanisms involved with accumulation and release of lead from cortial and trabelcular bone. A thorough investigation of bioavailability might include both types of measures, especially for a toxicant such as lead which accumulates during chronic exposure.

Bioavailability at the level of the target cell is, of course, independent of metal species or matrix but may present particularly interesting and complex experimental challenges. Cellular investigations have shown that toxic metal ions may bind with and alter blood cell membrane structure and function (Weis and Haug, 1989). X-ray microprobe analysis has shown qualitatively that synaptosomal mitochondria may accumulate lead (Silbergeld *et al.*, 1977). Quantitative estimates of bioavailability at the level of the mitochondria would further our understanding of the mechanisms of lead neurotoxicity. *In vitro* work has shown that, while much circulating lead is found bound to erthrocyte membranes, these cells may be limited in their binding capacity (Barton *et al.*, 1980). This may have important implications for those interested in modelling the biokinetics of lead distribution and dose at the target organ or tissue. Due to the potential saturation of erthrocyte binding capacity, and the resulting nonlinearity of the whole blood to plasma ratio, care must be taken when interpreting bioavailability studies involving large doses of lead. For example, elimination of lead may be more rapid when large doses are administered with a concomitant reduction in the proportional dose retained at a target site such as liver, brain or bone.

Choice of the Animal Model

Toxicological data derived from animal studies is often used for the purpose of extrapolation to humans. Only rarely is human low-dose exposure data of adequate quality and quantity available for risk assessment purposes. In lieu of adequate human data, choice of an animal model is the initial and most crucial step in the conduct of experimental investigations for the purposes of understanding relevance to humans. All subsequent assumptions regarding data interpretation and extrapolation will rely upon the depth of understanding which the investigator has regarding the model employed and its physiological, pharmacokinetic and biochemical similarity to humans. The USEPA acknowledges the importance of the model choice for the purposes of extrapolation to humans (Barnes and Dourson, 1988).

> "Presented with data from several animal studies, the risk assessor first seeks to identify the animal model which is most relevant to humans, based on the most defensible biological rationale."

Some considerations to be addressed when choosing an animal model for studies of bioavailability of lead (Pb) are presented in three categories. First, behavioral characteristics the experimental animal model will be introduced. Secondly, anatomical considerations will be addressed. Finally, the importance of physiological and biochemical differences will be discussed with particular focus upon developmental changes which are especially critical when assessing the bioavailability of lead. It should be recognised that, while it is convenient for the purpose of this paper to address each of the above as separate aspects to be considered when choosing an animal model, none should be considered in isolation.

Behavioral considerations

Rodents such as mice and rats, which are commonly employed as models for extrapolation to humans, are altricial species attaining an ability to thermoregulate at approximately 21 days of age. Recent studies indicate that rodents may retain a state of thermal lability following exposure to heavy metals including lead (Watkinson and Gordon, 1990). In response to xenobiotic insult, rats employ both behavioral and physiological mechanisms to lower body core temperature thus attenuating both the absorption of xenobiotic and the toxic response, with increasing potential for survival (Gordon, 1991).

Innate feeding behavior can greatly influence the bioavailability of lead. The presence of food in the stomach can clearly influence absorption of lead in humans (James *et al.*, 1985; Rabinowitz *et al.*, 1980). Rodents and lagomorphs are "continuous feeders" (Bivin *et al.*, 1979). Due to their continuous feeding habits the stomach of the healthy rat is never empty (Kraus *et al.*, 1984). Continuous feeding behavior allows for maintenance of gastric floral growth required by rodents and lagomorphs for digestion of cellulose and release of essential nutrients and vitamins from plant matter. It follows that both continuous feeding displayed by the experimental species and the presence of gastric flora may serve as a buffer for gastric fluid. Additionally, the presence of bacterial flora in the rodent or lagomorph stomach assures the continual presence of ligands for ionic lead in the form of negatively charged proteins, phytates and other phosphates. Such adaptive behaviour and physiology by rodents may retard the gastric dissolution of all forms of lead and other metals hence greatly reducing measurements of metal bioavailability. By contrast, canines and swine, like humans, tend to ingest periodic "meals" which are followed by gastric emptying. Complex regulation of gastric emptying by neural and hormonal mechanisms assures that delivery of gastric contents to the duodenum does not exceed the body's capacity to emulsify and process these contents.

At this writing, estimates regarding the amounts of soil which children ingest and the times of day during which ingestion events might occur are, at best, uncertain. It is likely that children are more exposed to environmental lead between rather than during, meals. Modelling the maximal exposure which might reasonably be expected to occur by assessing the bioavailability of lead-laden soil or other media on an empty stomach is only possible in species with periodic feeding behavior.

Rats and rabbits re-ingest fecal matter as an additional mechanism allowing for the digestion of cellulose and the absorption of essential nutrients and vitamins from

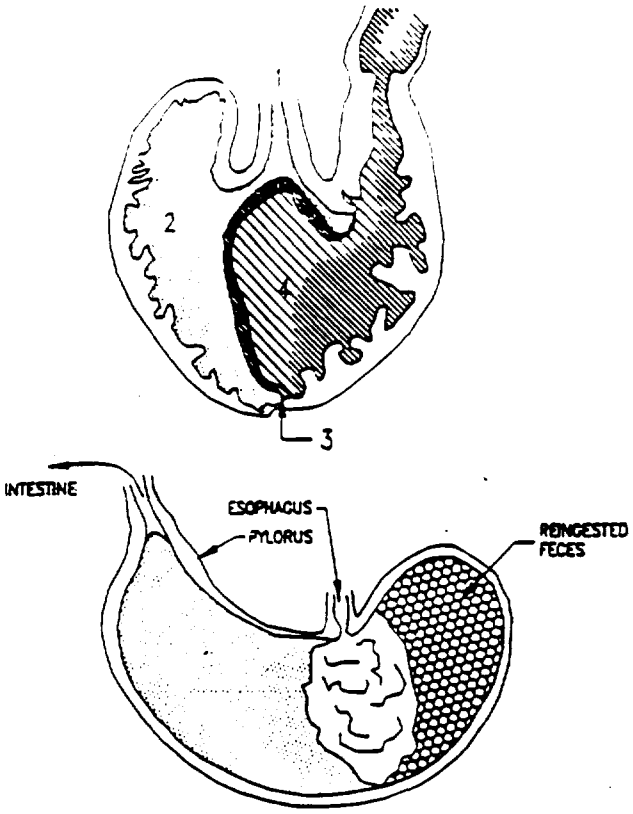

Figure 1 *Schematic representations of the rodent stomach: (a) Diagram of areas of the mucous membrane in the rat stomach; (1) cardiac region; (2) cutaneous (nonglandular) area; (3) line of transition from cutaneous to glandular mucous membrane; (4) cardiac glandular region (Hebel and Stromberg, 1976). (b) In the rabbit stomach ingested food is located in the pyloric region (1). Re-ingested fecal pellets are located in the large fundus (2) where they remain separated while fermentation proceeds.*

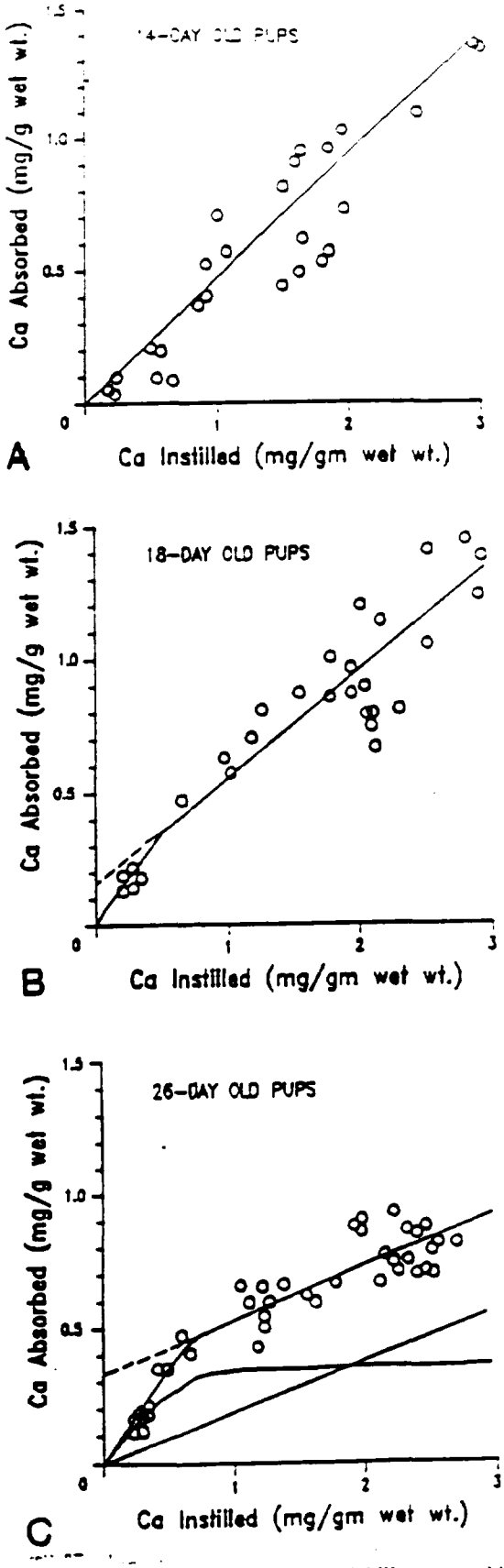

Figure 2 *Development of active calcium transport in the rat small intestine as measured using situ ligated duodenal loops. At 14 days of age (2a) calcium absorption occurs predominantly via passive diffusion across the brush border. At 18 days (2b) the initial development of active transport mechanisms is evidenced by curvilinear kinetics of the absorption curve at low dose and non-zero intercept at the ordinate. In the 26 day old rat (2c) both active (curvilinear) and passive (linear) components of the calcium transport are evident. From Dostal and Toverud (1984) with permission.*

material (Morot, 1911; Eden, 1940). This coprophagic behaviour displayed by rodents and lagomorphs creates problems for accurate determination of actual or relative measurements of bioavailability. Coprophagy introduces complications in the rodent model system since both essential nutrients and lead may be recycled (Thompson and Worden, 1956; Fullmer and Rosen, 1990). Without tedious and constant monitoring of the experimental rodent, the investigator can never be assured that measures of bioavailability are not biased by reingestion of previously excreted xenobiotic. Caging structures which deprive rodents from caprophagy may introduce uncertainties associated with mineral and vitamin

Table 1 *Comparison of the absolute and relative surface areas of the absorptive regions of the gastrointestinal tracts of humans and Rats. From DeSesso and Mavis (1989) with permission.*

Region	Human		Rat	
	Absolute surface area (m^2)	Relative surface area (region/body)	Absolute surface area (m^2)	Relative surface area (region/body)
Body	1.85	—	0.045	—
Stomach	0.0525	0.03	TBF[a]	TBF[a]
Small intestine	200	108	1.00	22
Duodenum	19[b]	10.3	0.08	1.8
Jejunum	138.6[b]	74.9	0.90	19.8
Ileum	42.4[c]	22.9	0.02	0.4

[a] TBF = To be found.
[b] Calculated using the data in Snyder *et al.* (1975), and proportion of mucosal surface area to length of intestine
[c] Calculated using the data in Snyder *et al.* (1975), and proportion of mucosal surface area to length as 20:1.

deficiency known to influence absorption of lead (Mahaffey-Six and Goyer, 1970). This experimental problem is greatly compounded by the rat's increased capacity for biliary excretion of lead discussed later in this paper.

Gastrointestinal anatomy and acid secretion

Discerning the role of gastric acidity in the bioavailability of various lead species is complex. Experimental background to fully understand the solution chemistry of metals in the stomach and anterior small intestine is not yet available. Active transport systems for calcium may also transport Pb across strong electrochemical gradients in the anterior small intestine shifting the solution chemistry far from equilibrium. As discussed above, the presence of gastric contents provides ligands for divalent metal ions, potentially influencing the bioavailability of lead across the gastrointestinal tract. For these reasons, equilibrium or pseudoequilibrium models of gastrointestinal solution chemistry are, at best, simplistic models with limited usefulness for the prediction of bioavailability. Experimental approaches to answering the question of the role of gastric contents might involve controlled comparisons of bioavailability in the presence and absence of gastric contents.

Gastrointestinal anatomy of the rodents has evolved to allow for digestion of plant material (Figure 1). Specialiaztion of gastric anatomy to accommodate the digestion of plant material may be expected to influence dissolution of less soluble metal salts in the stomach such as those found in mining related waste. Figure 1a depicts a schematic tracing from a sagittal section through a rat stomach. Unlike the human or swine stomach, the rodent possesses a relatively large aglandular forestomach with rumen-like mucusal folds. The forestomach in both rats and rabbits is covered with a stratified squamous epithelium which serves primarily as a reservoir for gastric flora and reingested feces (Figure 1b). The forestomach of the rat and rabbit is devoid of acid secreting capacity. This is in sharp contrast to the human stomach which is predominantly glandular and devoid of indigenous flora. The acid secreting region of the rodent stomach is restricted to a smaller area anterior to the pylorus. While little empirical information is available regarding the interspecies dif in total acid secretion, such differences might play a sig role in lead bioavailability. Further research into this a area should be encouraged.

Acid secretion by human parietal cells is regulat variety of nervous and hormonal stimuli (Kulchar Physiologically significant stimulants for acid secretion acetylcholine, gastrin and histamine. Acetylcholine released by vagal acuvity or by intramucosal refle directly on the parietal cell. Gastrin release is medi peptides or amino acids in the stomach. Distinct hi receptors have been located on parietal cell mem however, the exact mechanism for histamine release is n In all cases, stimulation of gastric acid secretion imping the glandular portions of the stomach. In rodents the g regions of the stomach represent a relatively small pc the overall glandular tissue in comparison with human:

In general, four experimental approaches to determ of acid secreting capacity have been applied. Measurer pH of gastric contents have been used to detect acid s capacity but this technique is unable to provide info about quantities of acid secreted over time or acid secre points (Garzon, 1982). Ussing chambers have been experimental techniques allowing for measurement o acid secretion and *in vitro* response to humoral stimuli *et al.*, 1981). Techniques involving gastric pylorus (Ikezaki and Johnson, 1983) and continuous saline p (Ackerman, 1982) have also been applied to the study o acid secretion. These latter techniques introduce the und experimental variables of reflex acid secretion and a respectively.

Little comparative information regarding the total cell mass in various experimental species is available acid output may be expected to be a function of pari activity or cell density, it is the overall parietal mass t relates to acid secretion during development (Yahav Since gastric acid plays an important role in the solubilization of various lead species, animal models parietal mass similar to humans would be the preferre

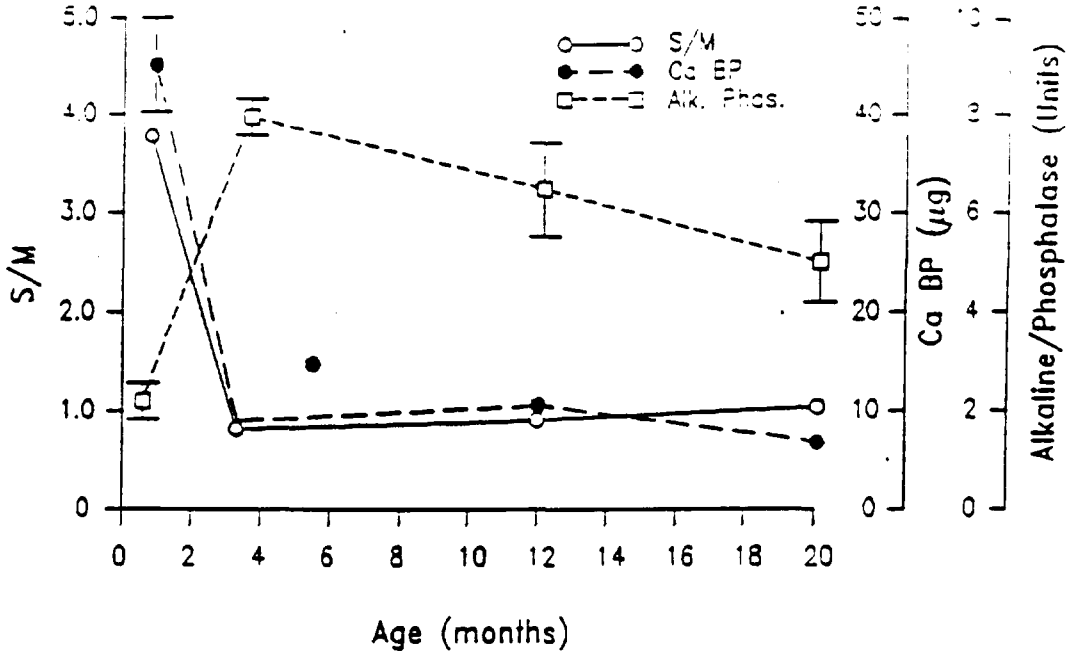

Figure 3 *Changes in duodenal calcium active transport, calbindin-D content and alkaline phosphatase as a function of age in Sprague-Dawley rats. Parameters were measured using everted duodenal sacs and active calcium transport is presented as serosal/mucosal (S/M) ratio of radiolabeled calcium. From Armbrecht et al. (1979) with permission.*

for the conduct of metal bioavailability studies. This choice might be particularly important for the investigation of lead species soluble only under acidic conditions.

Active absorption of lead occurs at the anterior portions of the small intestine. Relative length of major subdivisions of the small intestine in rats and humans is presented in Table 1. Large differences in intestinal length among various experimental species may be expected to influence both active absorption of lead and enterohephatic circulation.

Development of absorption mechanisms

Calcium is thought to cross the intestinal brush border by a variety of energy-requiring and energy-independent mechanisms. Reviews of this subject have been presented elsewhere (Wasserman and Fullmer, 1983; Toverud, 1989). Several investigators have proposed that Pb may share a common transport process with calcium (Mayaffey-Six and Goyer, 1970; Smith *et al.*, 1981; Gruden, 1975; Barton *et al.*, 1978). These processes may involve: (1) transcellular routes which include the involvement of the calcium binding protein, calbindin-D (intestinal calcium binding protein) and are saturable at 2–5 mM calcium; (2) paracellular routes which occur at higher concentrations and are diffusion dependent displaying linear absorption kinetics and; (3) proposed vesicular transport mechanisms. Calcium binding proteins involved in the absorption of calcium across the gut may have a higher affinity for Pb (Fullmer *et al.*, 1985).

Comparative investigations into the ontogeny of the calcium transport process provide important insights into our understanding of lead bioavailability. Such comparisons are essential to both design and interpretation of bioavailability studies of lead. Much evidence exists to suggest a link between developmental stage and absorption of lead in humans (Ziegler *et al.*, 1978; Alexander *et al.*, 1973; USEPA, 1986). Mechanistic understanding of the age dependence of calcium absorption has been most thoroughly investigated in rats (Dostal and Toverud, 1984; Pansu *et al.*, 1983; Armbrecht *et al.*, 1979; Mooradian and Song, 1989). Figure 2 presents the progressive development of calcium absorption in the rat intestine. Active transport mechanisms for calcium in the gastrointestinal tract of the developing organism parallel increased calcium requirement for growth of the long bones and development of muscle and nervous tissue. It is evident that in the pre-weaned rodent, active transport plays a minimal role in the absorption of calcium (Figure 2a). Shortly post weaning, however, the maturity of the active transport process is evidenced by the bi-phasic nature of the dose *vs* absorption curve (Figure 2b). A distinction between active and passive mechanisms for calcium transport in the intestine are evidenced by the curvilinear (active) and linear (passive) components of the dose *vs* absorption curve. In the low dose range, active transport processes for calcium are dominant (Figure 2c).

Of great significance for the conduct of bioavailability studies for Pb is the abrupt termination of intestinal active transport processes for calcium at maturity (Figure 3) (Armbrecht *et al.*, 1979 with permission; Mooradian and Song, 1989; Armbrecht *et al.*, 1980). At maturity development slows. Epiphyseal plates are sealed. The calcium requirement diminishes, and the gastrointestinal transport mechanisms for calcium respond accordingly. Figure 4 presents the relative growth and development of swine, rats and humans. Sexual maturity in the rat occurs at approximately 7 weeks of age. This

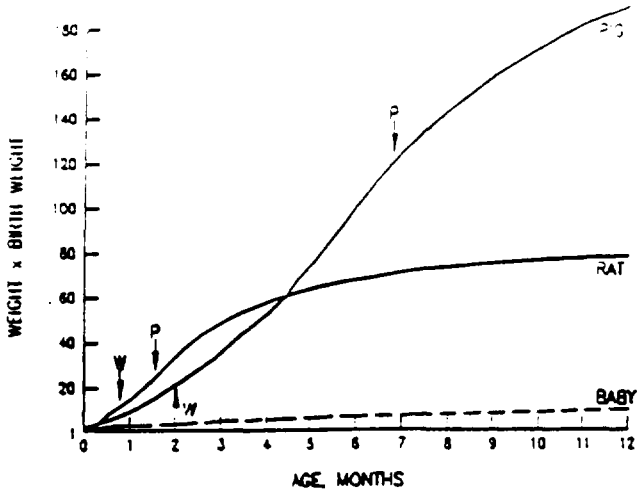

Figure 4 *Growth weight of rat, pig and human baby during the first year after birth. Birth weight = 1. From Widdowson (1968). W = Weaning; P = puberty.*

developmental milestone in rats occurs concurrently with cessation of active calcium transport. Assessment of bioavailability during or following the cessation of the active absorption component is inappropriate if an understanding of juvenile lead absorption is the intended purpose of the investigation.

The juvenile population is clearly defined as the population of most concern for exposure to environmental lead. It is likely that juvenile environmental exposure to Pb occurs in the low-dose range where active transport dominates the absorption process. If one presumes that Pb and Ca transport follow similar absorption kinetics, as the available evidence would strongly suggest, conduct of bioavailability studies for lead must be conducted on juvenile organisms.

The role of bile secretion

Fecal excretion of Pb via bile secretion and enterohepatic circulation can vary widely among various experimental species. Species differences in biliary handling of Pb may greatly influence measures of absolute or relative bioavailability. Comparative investigations of biliary excretion of lead in rats, rabbits and dogs have been conducted by Klaasen and Shoeman (1975). These investigations found profound species differences in the rates of biliary excretion of lead. Rabbits were found to excrete Pb via the biliary route at rates approximately one-half that of rats, while dogs displayed biliary excretion rates less then one-fiftieth that of the rat. Important physiological differences in biliary excretion have also been identified (Erlinger, 1987). The bile ducts alter the volume and composition of the bile fluid prior to entry into the digestive tract. Contribution of the bile ducts to overall bile flow is significant in the canines and primates but much smaller in rabbits, rats and guinea pigs. Bile acid transport in rats appears to be a saturable carrier-mediated process (Stremmel and Berk, 1986). Investigations into the bioavailability of Pb should consider the role of biliary excretion and enterohepatic circulation from a comparative perspective if sound estimates of bioavailability of lead in humans is the goal of the study.

Summary

The issue of lead bioavailability remains an important to an understanding of childhood exposure environmental hazard. The international pervasiveness problem, the sensitivity of the juvenile population apparent persistence of neurologic endpoints of lead tox contribute to the need for reliable estimates o bioavailability. In establishing estimates of lead bioava toxicologists are obligated to apply all available info regarding the comparative behavior, anatomy, physiol pharmacokinetics of the experimental model being em Much of the information available regarding the m mechanisms of lead absorption and toxicology has been from studies conducted using rodents. Some investigatc questioned the use of rodents for the purpose of unders the molecular aspects of lead and calcium metabolism uncertainties regarding the extrapolation to humans and Rosen, 1990). Other investigators continue to rodents for the purpose of understanding the absorpt distribution of lead (Killinger, 1990).

Cost and difficulty in handling are clearly recogr real world constraints to the conduct of animal re Regardless of the species employed to assess the biokir lead absorption and distribution, a comprehensive ass of the model being employed and its relevance to huma be incorporated into estimates of bioavailability. Withc an assessment, missrepresentations and missunderstanc the bioavailability of lead will be risked.

We believe that the weight of evidence sugge studies of metal bioavailability, particularly lead bioava studies, conducted in rodents or lagomorphs should be with caution. Evidence presented in this chapter which caution in the interpretation of bioavailability studies cor in rats and rabbits includes: (1) coprophagic and con feeding behaviour of these model species; (2) difficu assessing important developmental aspects o bioavailability in rats and rabbits; (3) evidence for re high rates of bile excretion of lead in rats and; (4) pr anatomical differences between these species and h Better model species are readily available for the study c bioavailability. More complete characterization o alternative models should be encouraged.

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Effect of Soil Dose on Bioavailability of Lead from Mining Waste Soil in Rats

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Abstract

The purpose of this study was to determine the extent of absorption of lead (Pb) in mining waste soil from Butte, Montana. It is the first study to fully investigate the bioavailability of lead in soils containing mine waste using a soil dose response approach. Young 7–8 week-old male and female Sprague-Dawley rats (5 animals/sex/group) were given mining waste soil [810 ppm lead (Test Soil I) or 3,908 ppm lead (Test Soil III)] mixed in a purified diet (AIN–76™) at four different dose levels (0.2, 0.5, 2 and 5% dietary soil) for 30 consecutive days. The test soil dose levels at 2 and 5% were chosen to bracket a pica-for-soil child's soil exposure levels. A pica-for-soil child is a young child who eats large quantities of soil (10 g day^{-1}). Standard groups included untreated controls and dosed feed soluble lead acetate groups (1, 10, 25, 100 and 250 μg Pb g^{-1} feed). The concentrations of lead acetate were chosen to bracket the test soil dose levels of lead. Liver, blood and femur, representing the three compartments in which lead is distributed in the body, were analyzed for total lead concentration using graphite furnace atomic absorption spectroscopy. Clinical signs, body weight, food consumption and liver weights for treated and standard groups were similar to control. Tissue lead concentrations from test soil animals were significantly lower than the tissue concentrations for the dosed feed lead acetate group. Group mean whole blood, bone and liver lead concentrations increased with increasing dose levels for most treatment groups. The increases in blood, bone and liver lead concentrations were not proportional with increasing dose levels and plateaued at the high dose levels. Relative percent bioavailability values, based on dosed feed soluble lead as the standard, were independent of the two different test soils, dose levels or sex, and only slightly dependent on the tissue (blood > bone, liver). Overall relative percent bioavailability values were 20% based on the blood data; 9% based on the bone data; and 8% based on the liver data (2 and 5% dose levels only). The results of this study will provide the scientific validity needed to determine the significance of lead exposure from Butte soils in assessing human health risks as part of the Superfund Remedial Investigation/Feasibility Study process.

Introduction

This study was initiated to address Superfund health risk assessment issues related to the bioavailability of soils containing lead from copper mining waste in Butte, Montana. The sources of lead representing potential risk to human health as identified by the Environmental Protection Agency are the waste rock dumps from previous underground mining activities which are scattered throughout the Butte area. Many of these dumps have been used over the years for residential fill material and have, therefore, become indistinguishably mixed with native soils. The results will provide the scientific validity needed to determine the significance of lead exposure from Butte soils in assessing human health risks as part of the Superfund Remedial Investigation/Feasibility Study process.

The objectives of this study were to determine the extent of absorption of lead contaminated mining waste soil using male and female Sprague-Dawley rats that were fed the mining waste soil mixed with AIN–76™ purified diet for 30 consecutive days. In addition to the mining waste soil treatment groups, a control group (purified diet only) and a standard group (dosed feed lead acetate) were included in the experimental design. At termination, blood, liver and femur specimens were collected from each animal for analysis of lead concentration using graphite furnace atomic absorption spectroscopy and/or inductively coupled plasma atomic emission spectroscopy. Relative percent bioavailability values were estimated by comparing tissue lead concentrations of the test soil to the standard treatment groups. This is a preliminary report of the findings of this study.

Methods

Materials

The original test substances were two mining waste soils (Test Soils I and II) with different lead concentrations that were composites of soils collected from residential areas in Butte, Montana. Test Soils I and II contained approximately 810 and 8,858 ppm lead, respectively. Test Soil II was not used because it had a higher lead concentration than wa targeted for this study. Test Soils I and II were blended together to produce Test

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Soil III which contained 3,908 ppm lead. Test Soils I and III were used for the dosed feed preparations. The pH of the soils was strongly to extremely acidic (according to USDA-SCS Soil pH Categories), with pH values of approximately 4.5 and 3.7 for Test Soils I and III, respectively. The particle sizes of the test soils were similar to the size of ingested soil particles that remain on hands (<100 μm) (Chaney *et al.*, 1989) and were of a size which optimized dissolution rate and extent of absorption. Lead (II) acetate trihydrate [$(CH_3CO_2)_2Pb{\cdot}3H_2O$] was used to prepare the dosed feed formulations for the standard group.

Test system and animal maintenance

This was a non-clinical laboratory study performed in compliance with the EPA Good Laboratory Practice Regulations, 40 CFR Part 792 (US EPA, 1989a). Seventy male and 70 female Sprague-Dawley rats (5 animals/sex/dose group; 7–8 weeks of age at initiation of dosing) were supplied by Charles River Laboratories (Kingston, NY). Animals were individually housed in standard polycarbonate cages, the dimensions of which (width × height × length) were 22" × 12.5" × 8". All animals were provided with deionized water *ad libitum* (<2.0 μg Pb L^{-1}) by glass bottle reservoirs fitted with stainless steel sipper tubes. All rats were fed *ad libitum* in metal feeders. The untreated control group animals were fed a purified diet [AIN-76™ complete meal (manufactured by Zeigler Brothers, Gardners, PA)]. The dosed feed soluble lead treatment group of animals were fed AIN-76™ sucrose-free meal into which the appropriate amount of sucrose and specific test substance, *i.e.* test soil or lead acetate, were added. The soil replaced part of the sucrose rather than replacing part of, or diluting, the complete mixed diet. The AIN-76™ complete meal and AIN-76™ sucrose-free meal had lead concentrations <0.20 μg g^{-1}.

Dosing regimen and administration

Dosed feed formulations were prepared for the animals fed lead acetate and the test soils mixed in the diet. The dose levels selected for use in this study were based on reported soil exposure levels for pica-for-soil children. For a 15 kg child with pica for soil, approximately 10 g of soil and 250 g dry diet are estimated to be consumed daily (US EPA, 1989b). Using these values, approximately 4% of the pica child's diet [(10 g soil/250 g diet) × 100] would be soil. Thus, dose levels of 2 and 5% soil in the diet were selected in this study to bracket the pica-for-soil child exposure level. The lower dose levels of 0.2 and 0.5% soil reflected logarithmic decreases from the higher dose levels down to the lowest exposure level that was believed to produce tissue concentrations just above the level of detection. Typical children (exclusive of those with pica for soil) ingest less than 100 mg of soil per day, on average, which is equivalent to approximately 0.04% soil in their diet (Calabrese *et al.*, 1989). Feeding rats a comparable dose would result in tissue levels indistinguishable from background levels. For the Test Soil I group, the 0.2, 0.5, 2 and 5% soil doses corresponded to 1.62, 4.05, 16.2 and 40.5 ppm lead. For the Test Soil III group, the concentration of lead in the four soil dose levels was 7.82, 19.5, 78.2 and 195 ppm. The exposure levels of the dosed feed soluble lead acetate group (1, 10, 25, 100 and 250 ppm) were chosen to bracket the estimated exposure levels for the two dosed feed test soil groups. Dosed feed concentrations, stability and homogeneity were verified

Table 1 *Actual concentration and percent target [illegible] dosed feed formulations*[a].

Formulation	Concentration (ppm) Target	Actual	Actual concentr. as a % of targ
Dosed feed soluble lead	1.0	1.11 ± 0.20	111
	10	10.3 ± 1.5	103
	25	27.1 ± 4.6	108
	100	98.7 ± 9.2	98.7
	250	242 ± 18	96.8
Dosed feed Test Soil I	1.62	1.63 ± 0.26	101
	4.05	4.31 ± 0.10	106
	16.2	17.4 ± 2.4	107
	40.5	38.9 ± 4.7	96.0
Dosed feed Test Soil III	7.82	7.97 ± 0.98	102
	19.5	22.6 ± 0.3	116
	78.2	75.7 ± 6.5	96.8
	195	183 ± 14	93.8

[a] For each mixed dose feed preparation a sample of e dose level was removed at the time of preparation (pr and at the conclusion of dosing (post-dose) for analys lead concentration. Triplicate samples were digested dose level per sampling period. Duplicate aliquots of digestate were analysed for lead by ICP or GFAAS. are reported as the mean ± SD of the pre- and post-d analyses of the two batches for each dose formulatior

during the study using graphite furnace atomic a (GFAA) or inductively coupled plasma (ICP) atomic technologies. The actual concentrations, as a percent for the different treatment groups averaged 103 ± dosed feed soluble lead group, 102 ± 5 for the Test So and 102 ± 10 for the Test Soil III group (Table 1). Tw of mixed feed preparations were refrigerated i containers for the duration of the 30-day study. Ap dosed feed mixtures were presented to the rats at appr the same time each day. Weekly body weights and d consumption values were used to determine actual dc

Tissue collection, preparation and analysis

Animals were euthanized with a single overdose o pentobarbital. Blood was collected into a syringe by puncture. Animals were necropsied and liver and b femur) were collected and frozen at approximatel Cardiac blood specimens remained refrigerated unti of preparation for analysis. Each blood sample was w on a rotating tumbler for at least 30 min prior to rem aliquot of known weight for lead analysis. Liver s were homogenised with tissue homogeniser (E Polytron, Westbury, NY) and frozen (approximatel until removed for analysis. The whole bone was pla NaOH to digest any residual soft tissue, dried and wei defleshed bone was then placed in 6N HCl unt completely solubilized. The completely solubili

specimens were frozen (approximately -20°C) until removed for analysis.

Samples were analysed using atomic absorption (Perkin-Elmer Model 5000 Zeeman atomic absorption spectrophotometer equipped with a Model 500 graphite furnace). Lead in all samples was calculated from linear regression equations using the method of standard additions. The method detection limits for the blood, bone and liver lead concentrations were 11.1 μg L^{-1}, 0.56 μg/g and 0.04 μg/g, respectively. The method detection limit is defined as the lead concentration that yields an absorbance equal to three times the standard deviation of a sample with a concentration of lead that is distinctly detectable above, but close to the blank absorbance measurements. All lead concentrations below the method detection limit were set at the detection limits prior to further statistical analysis.

Statistics

Nonlinear regression models were fitted to describe the relations between delivered doses (mg Pb kg^{-1} body weight) and tissue lead concentrations (μg L^{-1} or mg kg^{-1}). Regression models, incorporating background lead uptake, were fitted to the results from the standard group and from the test soil groups. Separate fits were carried out for males and for females. The relative bioavailability for a particular dose of a test soil was defined as the ratio of the lead uptake from that dose of the test soil to the lead uptake of the same dose of a standard treatment. Relative bioavailability estimates were based on the dosed feed standard. The lead uptake estimates from the test soil and from the standard were adjusted for background levels before comparison. The standard groups' regression curves were interpolated to obtain predictions at doses corresponding to the test group doses. The relative bioavailability calculation was represented as follows:

$$\text{Relative percent bioavailability} = R \times 100$$

$$R = [M_{tst}(X) - \beta_o]/[M_{std}(X) - \beta_o]$$

where,

X = dose (test or standard, mg kg^{-1} body weight)

$M_{std}(X)$ = model prediction for the standard

$M_{tst}(X)$ = model prediction for the test soil

(β_o) = overall background estimate

Results

Daily exposure index

There were no dose-dependent or treatment-dependent changes in body weight when compared to control group values for both sexes. Group mean body weight gain values for the various treatment groups were similar to control group body weight gain values. Furthermore, body weight gain results indicated that animals were thriving and growing during exposure to lead from either soluble lead acetate or soil lead mixed in the diet. After four weeks, group mean body weight gain values ranged from 27–40 g $week^{-1}$ for the males and 6–18 g $week^{-1}$ for the females. Thus, exposure occurred during a rapid growth phase and did not result in any overt toxicity based on body weight growth patterns.

The overall group mean food consumption value for the untreated control group rats during the 30-day in-life period was 23 g feed/day/animal. Group mean food consumption values for all treatment groups were similar to the control group values for both sexes. In addition, the data suggested that no palatability problems occurred with the dosed feed formulations.

Table 2 *Daily exposure index summary table*[*]

Treatment group	Targeted dose level (ppm)	Daily exposure index Males (mg Pb kg^{-1} BW)	Females
Dose feed soluble lead	1	0.0790	0.0960
	10	0.732	0.834
	25	1.86	2.01
	100	7.67	10.1
	250	16.8	26.2
Dosed feed Test Soil I	1.62	0.124	0.150
	4.05	0.314	0.501
	16.2	1.20	1.88
	40.5	3.36	4.40
Dosed feed Test Soil III	7.82	0.680	0.910
	19.5	1.67	2.31
	78.2	5.42	7.61
	195	12.7	23.8

[*] Dose levels were normalized to mg Pb kg^{-1} BW for the dosed feed groups. Normalization was performed using the following equation:

$$\text{Daily exposure index (mg Pb kg}^{-1}\text{ BW)} = \frac{\text{Group mean daily lead consumption for days 1, 8, 15, 22 (mg)}}{\text{Group mean body weight for days 1, 8, 15, 22 (kg)}}$$

The group mean daily lead consumption values were calculated by multiplying the concentration of lead in the dosed feed (ppm) by the daily food consumption.

The group mean daily exposure index values (mg lead consumed per kg body weight per day) for the male and female rats are summarised in Table 2. The group mean daily exposure index data indicated approximately proportional increases in the level of exposure (absolute amount and per body weight) at the different dose levels for each treatment group. The exposure index differed slightly between sexes for many of the dose levels of each treatment group, with the exposure level being higher for females than for males. The sex differences were attributed to similar group mean daily food consumption values between sexes but substantially lower body weight values for the female animals when compared to the male animals.

Tissue lead levels

Blood – Group mean whole blood lead concentration values for male and female rats were plotted *versus* dose in Figure 1. Overall, the group mean whole blood lead concentration values for the Test Soil I and III groups were significantly lower than the blood lead concentration values for comparable exposure levels of the dosed feed soluble lead. The group mean whole blood lead concentration values increased with increasing dose levels for all treatment groups but were not proportional,

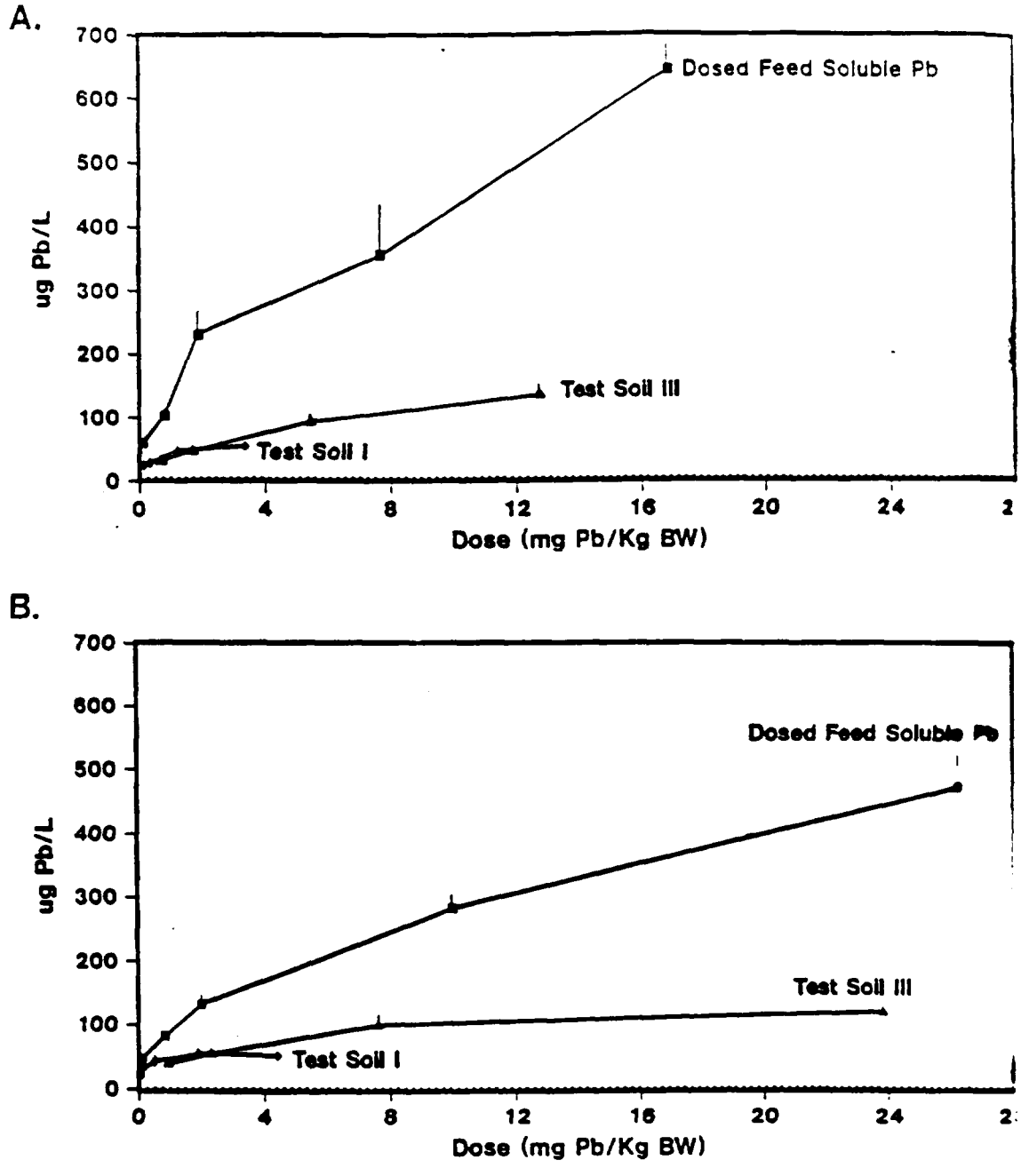

Figure 1 *Lead concentration in blood (µg Pb L^{-1}) versus dose (mg Pb kg^{-1} BW) in (A) male and (B) female rats. D expressed as the mean ± standard deviation. n = 5 (duplicate analyses per animal). Detection limit is 11.1 µg Pb*

reaching an asymptote at the higher dose levels in the soil treatment groups. A plateau was less apparent for the male and female dosed feed soluble lead groups. For the most part, similar group mean whole blood lead concentration values were observed for male and female rats within the same treatment group.

Bone – Group mean bone lead concentration values for male and female rats were plotted *versus* dose in Figure 2. The group mean bone lead concentration values increased with increasing dose levels for all treatment groups. Bone lead levels were very low following dietary ingestion of Test Soils I and III when compared to bone lead levels after ingestion of d soluble lead. Lead absorption and distribution into the detected after administration of dosed feed soluble le at all dose levels tested but only at the higher Test So dose levels tested. The increase in bone lead conc were not proportional with increasing dose levels. lead concentrations appeared to plateau at the higher for all treatment groups, although the plateau was les for the male dosed feed soluble lead group. For the similar group mean bone lead concentrations were of male and female rats within the same treatment gro

Liver – Group mean liver lead concentrations for

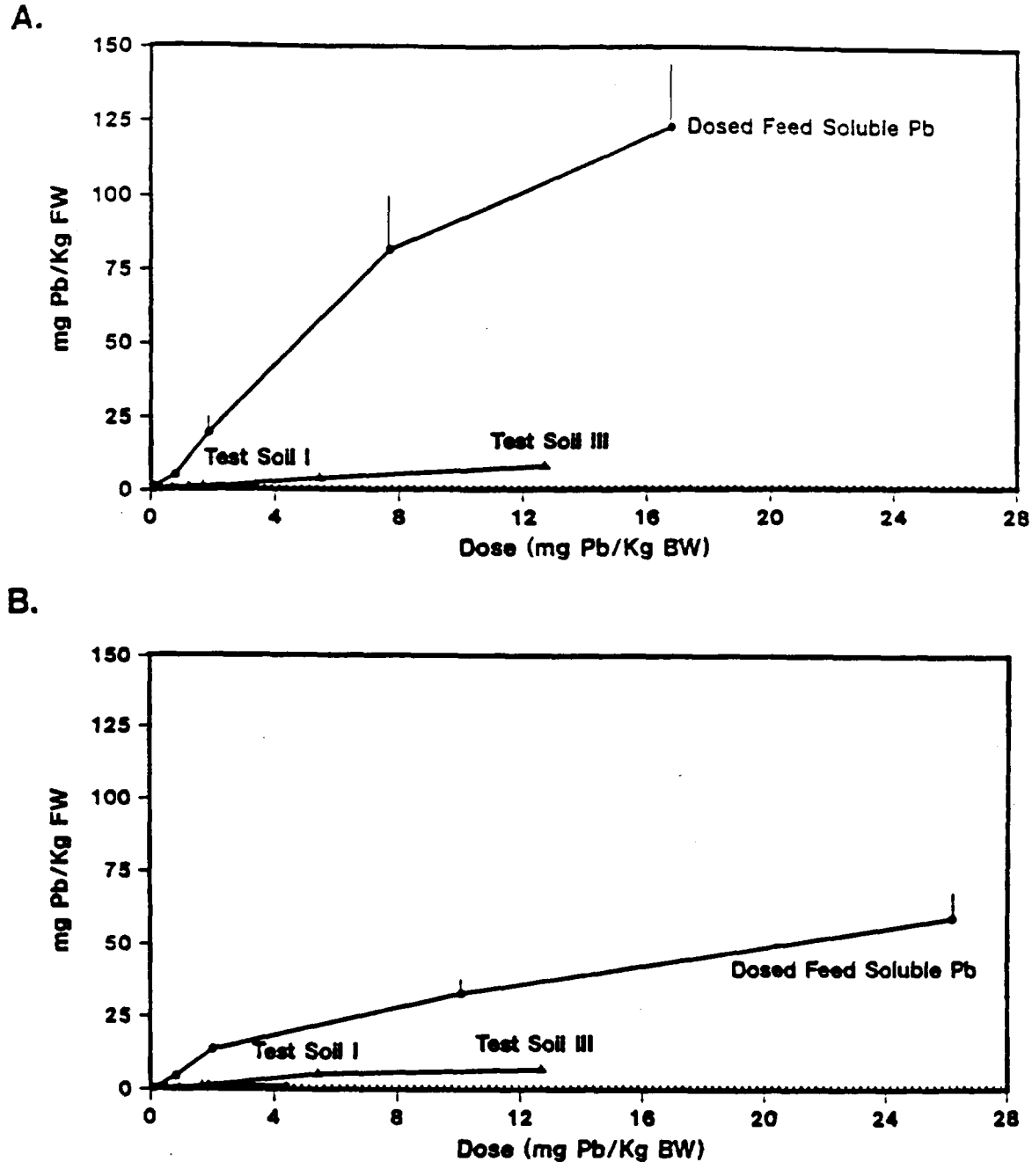

Figure 2 *Lead concentration in bone (mg Pb kg^{-1} FW) versus dose (mg Pb kg^{-1} BW) in (A) male and (B) female rats. Data are expressed as the mean ± standard deviation, n = 5 (duplicate analyses per animal). Detection limit is 0.56 mg Pb kg^{-1}.*

female rats were plotted *versus* dose in Figure 3. The group mean liver lead concentration values increased with increasing dose levels for the dosed feed soluble lead and Test Soil III groups. Overall, the mean liver lead concentration values for the Test Soil I and III groups were significantly lower than the liver lead concentration values for the dosed feed soluble lead groups. The increase in liver lead concentrations was not proportional with increasing dose levels and appeared to plateau at the higher dose levels for the dosed feed soluble lead and Test Soil III groups. Several of the animals in the 1 ppm dosed feed soluble lead group, the 0.2, 0.5 and 2.0% Test Soil I groups and the 0.2 and 0.5% Test Soil III groups had mean liver lead concentrations that were slightly above or not different from background levels. Similar group mean liver lead concentration values were observed for male and female rats within the same treatment group.

Relative percent bioavailability

Blood – Relative percent bioavailability values at the low dose levels (0.2 and 0.5%) had large standard error values which were attributable to the very low blood lead concentrations attained at these exposure levels. Thus, the extent of absorption of lead from the test soils and eventual accumulation in the

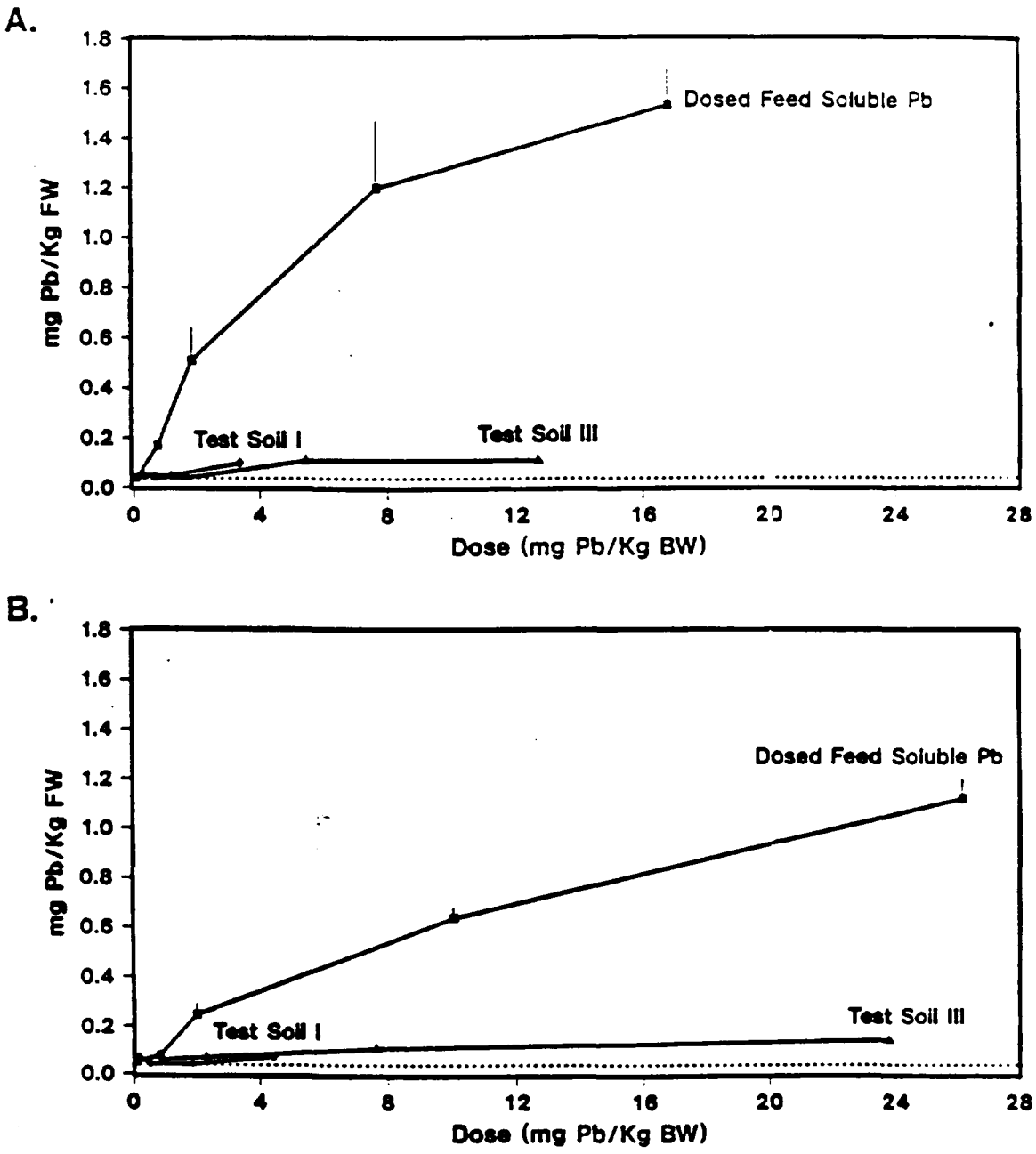

Figure 3 *Lead concentration in liver (mg Pb kg^{-1} FW) versus dose (mg Pb kg^{-1} BW) in (A) male and (B) female ra are expressed as the mean ± standard deviation, n = 5 (duplicate analyses per animal). Detection limit is 0.04 mg Pb*

tissues at these low levels could not be accurately determined. Only at the higher dose levels, *i.e.* 2 and 5%, were blood lead levels following Test Soil I and III ingestion sufficiently above background levels to allow bioavailability values to be confidently estimated (Table 3). Also, the 2 and 5% dietary soil dose levels bracket the pica-for-soil child's average daily soil ingestion. The 95% confidence intervals in these dose ranges were relatively tight. For Test Soils I and III, relative percent bioavailability values ranged from 12–26% and 20–27%, respectively, for the male and female 2 and 5% dose level groups based on the dosed feed soluble lead standard. There were no statistically significant differences between the dose levels or sexes. Using blood data, the overall mean percent bioavailability value for Test Soils I and III at soil in the diet was approximately 20%.

Bone – Relative percent bioavailability values at the levels (0.2 and 0.5% dietary soil) were highly variat standard error values) in a similar manner to the bloo percent bioavailability values. Data for the 2 and 5% d provided more reliable relative percent bioavailabili (Table 3). For Test Soils I and III, relative bioavailability values ranged from approximately 5–8–13%, respectively, for the male and female 2 and level groups based on the dosed feed soluble lead

There were no statistically significant differences between dose levels or sexes. Using bone data, the overall mean relative percent bioavailability value for Test Soils I and III at 2 and 5% soil in the diet was approximately 9%.

Liver – For Test Soil I, liver lead levels were slightly above or at detection limits at dose levels of 0.2, 0.5 and 2% dietary soil for both sexes. Thus, the extent of absorption and eventual accumulation of lead in the liver could not be accurately determined, making relative percent bioavailability estimates for these dose levels highly variable and imprecise. At the 5% dose level, the relative percent bioavailability values were approximately 9 (males) and 8 (females) percent based on the dosed feed soluble lead standard (Table 3). For Test Soil III, liver lead levels were near detection limits at dose levels of 0.2 and 0.5% dietary soil for both sexes. Thus, relative percent bioavailability estimates for the 0.2 and 0.5% dose levels were variable due to the relatively low absorption and accumulation of lead to the liver following ingestion of Test Soil III. For the 2 and 5% Test Soil III dose levels, group mean relative percent bioavailability values were approximately 7 and 8%, respectively, for the males and 14 and 10%, respectively, for the females, based on the dosed feed soluble lead standard (Table 3). The overall mean relative percent bioavailability value for Test Soils I and III at 2 and 5% in the diet was approximately 8%.

Table 3 *Relative percent bioavailability values of lead for male and female rats administered Test Soils I and III mixed with feed*[*].

Group		Test Soil I	Test Soil III
Blood			
Males	2%	18.1 (6.0)	19.6 (3.3)
	5%	12.1 (3.6)	21.5 (3.8)
Females	2%	25.7 (7.8)	26.8 (4.8)
	5%	13.8 (4.7)	22.1 (4.4)
Bone			
Males	2%	8.0 (3.5)	7.5 (1.4)
	5%	4.8 (1.5)	7.5 (1.4)
Females	2%	10.6 (3.3)	13.3 (2.2)
	5%	6.1 (1.9)	13.0 (2.6)
Liver			
Males	2%	4.3 (2.4)	7.1 (1.5)
	5%	8.7 (2.0)	7.5 (1.5)
Females	2%	0.6 (3.1)	13.6 (3.1)
	5%	8.2 (2.8)	9.8 (2.1)

[*] Relative percent bioavailability values were determined using the dosed feed soluble lead group as the standard. Tabled data are reported as the mean with the standard error of the mean in parentheses.

Discussion

This study was conducted to determine the extent of absorption (relative percent bioavailability) of lead from two different mining soils using Sprague-Dawley rats fed on soil mixed with a purified diet. It is the first study to fully investigate the bioavailability of lead in soils containing mine waste using a soil dose response approach. Male and female Sprague-Dawley rats (5 animals/sex/group) were fed mining waste soil from Butte, Montana (810 and 3,908 ppm lead) mixed in an AIN-76^{TM} purified diet at four dose levels for 30 consecutive days. The soil was mixed with a purified diet to lower the background levels of lead found in the control animals and to allow the detection of the soil-derived lead in the animals' tissues even at low lead levels. The nutritionally complete purified AIN-76^{TM} diet (Bieri *et al.*, 1977) is less likely to inhibit lead absorption than regular rat chow. In addition, purified diets more closely simulate the low-fibre diets of most US citizens than do rat chow diets.

The rat was used because it is considered an acceptable model for human risk assessment (National Research Council, 1983) and is the preferred species for metabolism and pharmacokinetic studies performed under the Toxic Substances Control Act (TSCA) (US EPA, 1982). In addition, the food consumption patterns and stomach pH of rats and young children are similar (Chaney, 1991). For example, rats and young children generally eat intermittently and frequently while they are awake. The pH in the rat stomach ranges from 2.6–5.1 which is similar to the pH range found in children's stomachs after they have eaten. The age range and developmental state of the rats in this study also support their use in prediction of lead uptake in children. The rats used were 7–8 weeks old at the start of dosing. These were young growing rats as indicated by the increases in their body weight. The males gained about 125 g (36% increase) and the females gained about 45 g (21% increase) over the time period studied. At the start of dosing, these animals were not sexually mature. In this strain, vaginal patency generally occurs at about 5–6 weeks of age. Sperm production is observed at about 9–10 weeks and, to obtain adequate sustained pregnancies, this strain is generally not mated until they are at least 10–12 weeks of age (personal communication, Joanne Killinger, 1991).

The study was 30 days in length because of the long biological half life of lead. Thirty days appeared to be an adequate compromise between the need for sufficient time for the accumulation of lead in the blood and tissue, while still balancing the need for an exposure period which ensured that animals remained in a rapid growth phase. The target tissues measured were whole blood, liver and bone, thus representing the three main compartments in which lead is distributed in the body.

The dose levels selected for this study were based on the soil levels reportedly ingested by pica-for-soil children. A 15 kg pica-for-soil child might ingest as much as 10 g of soil as part of a daily 250 g diet (approximately 4% of the dry diet). The 2 and 5% soil dose levels bracket the pica-for-soil child exposure level, and the relative percent bioavailability values were based on these two soil dose levels. Normal children (exclusive of those with pica for soil) ingest less than 100 mg of soil per day (Calabrese *et al.*, 1989). The dose levels of 0.2 and 0.5% soil were logarithmic decreases from the higher dose levels to the lowest lead level detectable above background in rats fed a purified diet. The dose levels of the lead acetate standards were designed to bracket the soil lead dose levels.

The clinical appearance, body weight, food consumpuon and liver weight values in the soil-treated animals were similar to those in the control group animals, indicating no overt toxicity that may have affected the relative percent bioavailability values esumated for this study. Significantly higher lead concentrauons were measured in the blood, bone and liver of animals fed dosed feed soluble lead when compared to animals fed the test soils mixed in diet. Thus, under comparable dosing conditions, the bioavailability of lead in the Butte soils was considerably less than that of lead acetate administered in the diet. Over the dose range tested (0.2–5% soil in diet), blood, bone and liver lead concentration *versus* dose profiles generally plateaued for animals of both sexes when fed the test soils mixed in diet. The plateau response to soil lead is extremely apparent if one compares the pattern of response to tissue lead for the soil animals to the higher linear slope at the start of the lead acetate curves. These data are consistent with results from epidemiological studies that show there is a weak relationship between soil lead concentration and human blood-lead levels at other mining sites with a high proportion of lead sulphide in the mineral assemblage (Bornschein *et al.*, 1990).

Relative percent bioavailability values, based on dosed feed soluble lead as the standard, were independent of the two different test soils, dose levels or sex, and only slightly dependent on the tissue (blood > bone, liver). Lead acetate in the diet is an appropriate comparison because lead acetate is highly soluble (thus maximizing bioavailability) and can serve as a surrogate for lead compounds ingested in the human diet. Overall relative percent bioavailability values (assuming no biologically significant differences between the sexes, dose levels or soils) were 20% based on the blood data; 9% based on the bone data; and 8% based on the liver data (2 and 5% soil dose levels only). The low bioavailability of lead in the Butte soil-treated animals agreed favourably with low blood-lead levels (average of 3.5 $\mu g\ dL^{-1}$) found in children from Butte, Montana (Butte–Silver Bow County Environmental Health Study, 1991). Negligible lead absorption (*i.e.* only slightly above background concentrations) occurred at test soil dose levels of 0.2 and 0.5%. These lower dose levels, although more closely approximating soil-lead exposure to normal children, were still above the lead level intake of a normal child. Thus, uptake of lead from soil at dose levels similar to those for a normal child's exposure would not be detectable under this study protocol.

The findings of this present study have significant implications for assessing risks to young children from lead in mining waste soils and, by extrapolation, on the clean-up levels that will be protective of human health in communities where the main source of soil lead is due to mining and milling activities.

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Selected Chemical and Physical Properties of Soils and Gut Physiological Processes that Influence Lead Bioavailability

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Abstract

This paper considers selected field examples of physical and chemical properties of soil and some of the interactions with gut physiological processes that are related to lead bioavailability. The blood lead response to quantity of lead in mining and milling environments compared with urban and lead smelter conditions appears to be different. The emphasis of this paper is to understand the complexity of the urban environment.

Bioavailability appears to be related to physical and chemical qualities other than mere quantity of lead. Particle size is one physical quality that influences bioavailability. Compared to intact lead–based paint, small particle emissions from vehicles govern the general soil lead pattern in urban environments. Lead has accumulated in soils in proportion to city size, with the inner–city generally measuring the highest lead levels. The soil lead situation is further exacerbated by the chemical influence of other toxic substances such as zinc. In several cities, zinc levels of 1,500 ppm and higher plus acid conditions (pH 5.4 and lower) have been observed. This condition is phytotoxic to plants and the deficiency of plant cover increases the likelihood for soil lead ingestion. After ingestion, nutritional status becomes an important factor with both iron and calcium deficiencies increasing lead bioavailability.

To complement the other discussions of the GI tract and bioavailability in this volume, the following physiological responses of the gut that either increase or decrease soil lead bioavailability are described: (1) The role of the normal microbial flora in altering baseline gut function, (2) effect of pH, (3) intestinal transit time, (4) role of mucus, and (5) barriers to lead transport. Physiologically there are nine physical and/or chemical barriers to soil lead absorption which tend to decrease bioavailability; any breakdown of or increased permeability in these barriers would have the opposite effect. The addition of a soil amendment, such as pathogen free processed sludge, would be expected to be a practical means for reducing soil lead bioavailability. The amendment should serve to bind lead and thus increase effective particle size. It would also have the benefit of improving plant growth as shown in the laboratory. Further study is needed to conduct toxicity testing and undertake field evaluation.

Introduction

The risk of exposure of children to excessive soil Pb varies widely. The Pb concentration of soil is only one measurable characteristic and the degree and variation of bioavailability of Pb in soils and dusts likely involves several variables. At the very least these include: (1) the chemical and physical differences of the Pb sources; (2) the characteristics of the soil media and the many chemical, physical and biological differences that interact with Pb in a particular soil; and (3) the complexity of physiological apparatus of animals for ingesting, digesting and absorbing Pb that enters and passes through the digestive tract. This paper addresses selected field conditions that directly pertain to these issues.

Environmental Lead Sources and Their Role In Bioavailability

Lead mines, mills, lead smelters and urban soils

There appear to be major exposure variables which differ between several main soil Pb contamination situations, tailings from lead mines and milling sites, smokestack emissions from lead smelters, and urban sites (Steele *et al.*, 1990). Within these situations the blood Pb response by humans to the Pb of soils appears to differ. Mining and milling materials contain large quantities of Pb, but the blood Pb response to mining materials appears to be relatively small. In contrast, the blood Pb response is relatively large to smaller quantities of soil Pb near smelters and within inner–city environments. There are both physical and chemical differences between Pb sources within mines and mills, smelters and urban environments that may account for the observed variations. For example, if the Pb is in the form of a sulfide it is commonly assumed that the Pb is less bioavailable than when it is in the form of a carbonate or oxide (Steele *et al.*, 1990; Chaney *et al.*, 1989). But it has been long known that lead sulfide is slowly soluble in gastric juices (Woelfel and Carlson, 1914; Healy *et al.*, 1982). Recent dietary studies do not show a difference in bioavailability between soluble lead compounds such as lead nitrate and lead cysteine compared with insoluble fine particle lead sulfide (Rabinowitz *et al.*, 1980). Large interpersonal variability has also been noted (Rabinowitz *et al.*, 1980).

An alternate explanation for the differences in response at various sites may be related to the characteristics of a specific source of Pb. Particle size plays a major role in bioavailability. The smaller the particle the more effective it is in gaining physiological entrance into the organism (Barltrop and Meek, 1979; Woelfel and Carlson, 1914; Chaney *et al.*, 1989). Field surveys provide information about the properties of soil Pb that contribute to bioavailability. In the next sections, physical and chemical conditions are emphasized that might account for the differences in the urban environment.

The quantity of lead used in consumer products

Millions of tons of Pb have been used in the USA in the form of paint and additives to gasoline. Since 1910, the amount of Pb used in paint accounts 4.9 million tons (43%) compared to the amount of Pb used as a gasoline additive or 6.5 million tons (57%). In addition another two million tons or so of Pb were used in paint prior to 1910. Pb use in paint peaked in the 1910s and 1920s and declined rapidly during the 1930s and 1940s. The use of Pb in gasoline escalated rapidly during the 1940s and 1950s and again in the mid-1960s, peaked in the early 1970s, and then declined rapidly to its current level. Major urban centers are where the Pb exposure problems are most severe and require the most emphasis (ATSDR, 1988, Charney *et al.*, 1980, Mushak *et al.*, 1990, Patterson, 1980). The pattern of use and the physical properties of lead–based paint and leaded gasoline differs in ways that strongly influences the impact that each source has on urban soils.

Lead–based paint as a potential and actual hazard

Lead–based paint predominated during the 1910s and 1920s when housing construction was undertaken in locations along major railroad routes. There are approximately 42 million housing units that contain lead–based paint located in residences in farms, small towns and large cities in all parts of the nation (ATSDR, 1988). The amount of Pb contained in the paint was directly related to the cost of the paint. Older homes in historically affluent communities are likely to contain more Pb than older homes in historically poor neighborhoods. Most of the Pb used in paints probably remains attached to the interior surfaces where they were originally applied. The condition of lead–based paints on exterior surfaces is probably more variable and depends on type of paint, degree of weathering and the maintenance frequency that a particular house may receive. When lead–based paint deteriorates or is removed from the building exterior it accumulates in the soils around the building and becomes an actual hazard.

As an intact coating, lead–based paint is a potential hazard that measures 300,000 ppm Pb and even higher. When paint chips are reduced in particle size to less than 50 µm (Barltrop and Meek, 1979) they become markedly bioavailable and an actual hazard. Thus, lead–based paint is generally a potential hazard when intact and becomes a major problem when it is abraded into small particles by sanding and burning (Amitai *et al.*, 1987; Marino *et al.*, 1990; Sayre, 1987).

In a recent report, age of home was used as surrogate data for environmental exposure in order to calculate the degree of Pb exposure of children in various U.S. communities (Florini *et al.*, 1990). The surrogate data does not agree with empirical data from old communities of five Minnesota communities. The hypothesized relationship between age of home and degree of childhood Pb exposure is not supported. The amount soil is a function of city size and childhood exposur the pattern of Pb in soil and not age of homes (Mie 1989, Mielke in press). The accumulation of Pb dust environments and exposure of children is related processes than simple occurrence of lead-based pain

Lead dust from traffic as an actual hazard

The potential health hazard of Pb additives in gase foreseen in the 1920s (Rosner and Markowitz, 1985; L 1990) and the actual accumulation was empirically so the USA (Angel *et al.*, 1975; Angle and McIntire, 19 *et al.*, 1983; Earickson and Billick, 1988), Ne (Shellshear *et al.*, 1975), Britain (Thornton Australia (Day, 1977; Fergusson *et al.*, 19 concentration is highest in the biggest cities inner–cities and least in small towns and rural lo *et al.*, 1984/85; Mielke *et al.*, 1989; Chaney and

The particles of the Pb emitted from stratified into two size categories; 40% of the em mass median diameter greater than 10 µm, and emitted Pb has a mass median diameter less than EPA, 1986). The larger particles generally settle dust within 100 m of the road while the smaller entrained in the air as aerosols and transported The aerosol portion may settle out either by by precipitation or by impaction on surfaces Buildings are suitable surfaces for impaction for about half the amount of Pb accumulated buildings (Mielke *et al.*, 1984; Chaney and From the empirical data of the cities of M that the major accumulation of Pb was emi vehicles. Furthermore, the accumulated Pb appears to be the major bioavailable source of (Mielke *et al.*, 1983; Mielke *et al.*, 1989; M 1989).

Other factors also play an important role as individual susceptibility, socioeconomic status, conditions of the immediate home and community awareness. Of particular importance such as nutritional status, especially iron, calcium and time since the last meals (degree of fasting). These fa be described as a part of the factors which influe bioavailability of Pb in the gastrointestinal tract.

Soil zinc as a factor in lead bioavailability

Other toxic substances have also accumulated in so same pattern as Pb, and these may exacerbate the poss becoming exposed. Inner–city soils are often barren or covered with vegetation, even in humid environments. plant cover is a characteristic that influences the probab Pb in soil might be available for ingestion by chi addition to Pb, one feature of urban soils is the occur unusually high amounts of Zn (Mielke *et al.*, 1983; *et al.*, 1984). Zinc influences the quality of plant grow

Zinc is used in the manufacturing of tires and is an to motor oil. Together, these two uses of Zn are suff account for a large amount of the urban soil accumu this metal. Zinc is generally recognized as a required n for animals and in fact has been cited as being defi humans (Prasad, 1983). On the other hand, th

consequences of excessive Zn to plants is well-known.

Zinc toxicity for plants depends on soil pH and the amount of Zn in the soil. According to the USDA/Soil Conservation Service soil pH categories, a soil is strongly acid when the pH is 5.1–5.5. When the soil is strongly acid, pH 5.2–5.4, most plants cannot tolerate more than 1,500 ppm Zn (Chaney *et al.*, 1990). Only a few plants, a red fescue cultivar 'Merlin', barley, and several tall fescue cultivars, are resistant to elevated levels of Zn. Most other monocotyledonous and dicotyledonous species are Zn intolerant.

The urban pattern of soil pH has been described for garden plots of the city of Baltimore (Mielke *et al.*, 1983). In Baltimore, there is no clustering of soil pH within any part of the city. All parts of the city had vegetable garden soils with nearly an equal chance of being either alkaline or acid. About 20 percent of the garden soils had a strongly acid soil pH (less than 5.5). Also, in the inner-city of Baltimore, about 20% of the soil samples were above 500 ppm Zn. The Baltimore vegetable garden soils were assumed to be mixed to a depth of about 15 cm and the depth of mixing dramatically dilutes the metal concentration compared to what is normally within the top 2 cm of the soil. In Baltimore, the same inner-city soils that had elevated Pb levels also had elevated Zn levels *and* the possibility of strongly acid soil conditions. Several studies indicate higher levels of Zn within 2 cm of the soil surface.

In London, soils have been recorded with Zn levels of 1,562–2,182 ppm (Thorton, 1990). Car parks in Lancaster (UK) have Zn levels of 1,010–3,725 ppm (Harrison, 1979), and in Hong Kong, surface soils of roadside parks have an average Zn concentration of 1,281 ppm and a range of 173–11,316 ppm (Tam *et al.*, 1987). The above examples illustrate the fact that urban soils can be both strongly acid *and* have a Zn concentration of around 1,500 ppm or more. Under those conditions phytotoxicity is a problem. Chemical conditions that weaken or diminish plant growth also increase the likelihood of soil ingestion which, in turn, enhances bioavailability. In the next section, selected physiological processes which affect Pb bioavailability are discussed.

Gut Physiological Processes Affecting Lead Bioavailability

Nutritional influences: iron and calcium deficiency

It is well known that dietary deficiencies can increase Pb bioavailability. Epidemiologically, the NHANES II study (Mahaffey and Annest, 1986) showed that Fe deficiencies can increase Pb bioavailability and should be accounted for when screening populations for public health risks. Also, Six and Goyer (1970) showed in a rat-feeding study that low dietary Ca levels increased Pb toxicity. Thus, once ingested the relative toxicity of a given amount of Pb will depend upon the nutritional status of the persons at risk.

Role of the 'normal' microbial flora

The 'normal' microbial flora influences base-line intestinal epithelial cell function, and will impact Pb absorption and bioavailability. Flora factors which are likely to be important have been recently reviewed (Heneghan, 1988) and can be summarized as follows: short chain fatty acid production by colonic bacteria provides nutrients for colonic mucosal cells and indirectly affects the ability of the colon to absorb Pb; increased acid production by colonic bacteria tends to lower pH and may increase the bioavailability of Pb; the oxidation–reduction potential in the colonic lumen is much lower in conventional rats, -175 mV, compared to germfree controls, +75 mV, which can influence the chemical form of the Pb in the lumen; dietary fiber and the flora's metabolic alterations of it may influence the amount of fluid in the colon and increase or decrease the length of time lumenal contents with Pb will remain in the colon with a corresponding increase or decrease in Pb absorption.

Effect of pH

In general, a lower pH or higher acidity means increased soil Pb bioavailability. However, stomach pH or acidity may vary by a factor of 10,000 between the extremes of 1.5, a common fasting level, to 5.5, a common level when mealtime food is present. Thus, the amount of soil Pb which is bioavailable will be determined by how full or empty the stomach is when the Pb is consumed. Furthermore, soil can buffer stomach acid and help prevent lower pH of gastric contents. Thus, poor inner-city children who may eat less and frequently skip meals would lack buffering capacity and have a lower stomach pH. These children would be expected to exhibit higher Pb bioavailability. The rest of the GI tract from the stomach to the colon, the small intestine, has a relatively neutral pH around 7.0. However in the colon, the pH is again lower (pH about 6.5), due to the presence of the colonic microbial flora, which produces large quantities of short chain fatty acids which in turn provide nutrients for colonic epithelial lining cells.

Intestinal transit

Slower intestinal transit, the time for passage through the intestinal tract, allows increased time for exposure of the soil Pb to the acid environments of both the stomach and colon. There are many factors which will increase or decrease the time which Pb containing intestinal contents remain in these two organs. For example, fatty meals inhibit gastric emptying and would therefore increase the time of exposure of Pb to gastric acid. On the other hand increased dietary fiber, which increases the water content and bulk of fecal contents promotes colonic emptying and would, therefore, reduce the time colonic Pb contents would be exposed to a lower pH.

Role of mucus

Mucus acts like the skin of the alimentary tract and it serves as effectively as, and in a more versatile way than, the skin of the body. In 1856, Claud Bernard commented that "mucus encloses the gastric juice like a vase as impermeable as if it were made of porcelain." Mucus does indeed form a coherent protective layer covering the living lining of the alimentary tract, and its integrity in health prevents both bacterial infection and biochemical damage. At the same time, it allows the regulated movement of simple molecules that will pass into the absorbing cells. Recent research with microelectrodes (Bahari *et al.*, 1982) has identified a hydrogen ion concentration gradient across the mucus on human gastric mucosa due to bicarbonate secretion by the epithelial cells; these data support the hypothesis that a 'mucus–bicarbonate' protective barrier exists.

Elevated levels of mucus (Loesch, 1968), of amino acids that are typical of mucus (Combe and Pion, 1966) and of hexosamine have been found in the cecal contents of germfree rats and mice, compared to their conventional counterparts.

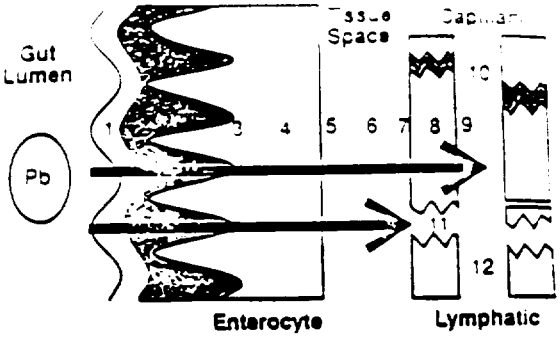
Lindstedt *et al.*, (1965) demonstrated a five-fold increase in the concentration of hexosamine in the cecal contents of germfree rats when compared to their conventional-controls. Furthermore, this excess of mucus and related substances may contribute to the inhibition of water absorption and the increased liquid contents of the lower alimentary tract of gnotobiotic rodents (Csaky, 1968).

Barriers to lead absorption

The gastrointestinal tract is not a simple dialysis tube which conveys food through the body but rather it is a very complex organ system which helps to maintain homeostasis, a steady-state of physiological health. As a result, there are many barriers, both physical and chemical, which tend to keep food and soil/dust Pb trapped within the intestine and thereby reduce Pb absorption and reduce soil Pb bioavailability. Some of these barriers, which are present throughout the entire length of the GI tract are shown in Figure 1 (not drawn to scale).

When a compound containing Pb inside the gut tries to pass into a capillary (Figure 1, number 10), at least nine barriers are crossed, due to the tightness of the junctions between the capillary endothelial cells: (1) the unstirred layer of water molecules, through which all substances must diffuse across to be absorbed; (2) the mucus layer and glycocalyx, a gel layer coating which protects the gut lining; (3) the microvilli membrane of the enterocyte, the epithelial cells lining the GI tract; (4) the enterocyte cell body; (5) the basement membrane surface of the epithelial cell; (6) the tissue space; (7) outer capillary endothelial cell membrane; (8) endothelial cell body; (9) endothelial cell membrane lining the capillary. On the other hand, if the lead molecule heads towards a lymphatic vessel (Figure 1, number 12), only the first six barriers are encountered, because there are large spaces (Figure 1, number 11) between lymphatic endothelial cells.

One measure of the importance of these barriers is the fact that the entire gut epithelial cell lining (Figure 1, barrier numbers 1–4) is replaced with new cells every 2 to 4 days throughout life. Furthermore, conditions which compromise this barrier are likely to increase soil Pb bioavailability, such as: very young age (the younger a person, the less well developed are their intestinal barriers), malnutrition, hyperacidity, decreased enterocyte cellular renewal, and impaired mucus metabolism.



BARRIERS TO LEAD ABSORPTION

Figure 1 *Diagram of the anatomical and physiological barriers across which substances containing lead must in order to reach a capillary or lymphatic vessel. Not to scale. See text for key to numbered barriers.*

Other factors

In addition to these basic physiological barriers to bioavailability, a person's life style and the substance compounds come in contact with will also influence When a dose of soil Pb enters the GI tract, the following influence its bioavailability: a long fasting interval skipping meals) increases acidity and increases the (Rabinowitz *et al.*, 1980); the presence of food a acidity and may bind the soil Pb thereby decreasing absorption; constipation, on the other hand, will keep soil Pb in the colon longer, exposing it to the slightly environment created by the colonic microflora increasing the time available for colonic absorption of Pb can come into contact with other substances (food a in the gastrointestinal tract that bind Pb and make bioavailable.

Soil Amendment and Lead Bioavailability

Amendments could be utilized beneficially to bind Pb and possibly reduce soil Pb bioavailability. An appropriate amendment would also serve to decrease the influence chemicals such as Zn phytotoxicity. The concept of a PFRP (Processes to Further Reduce Pathogens, 40 C

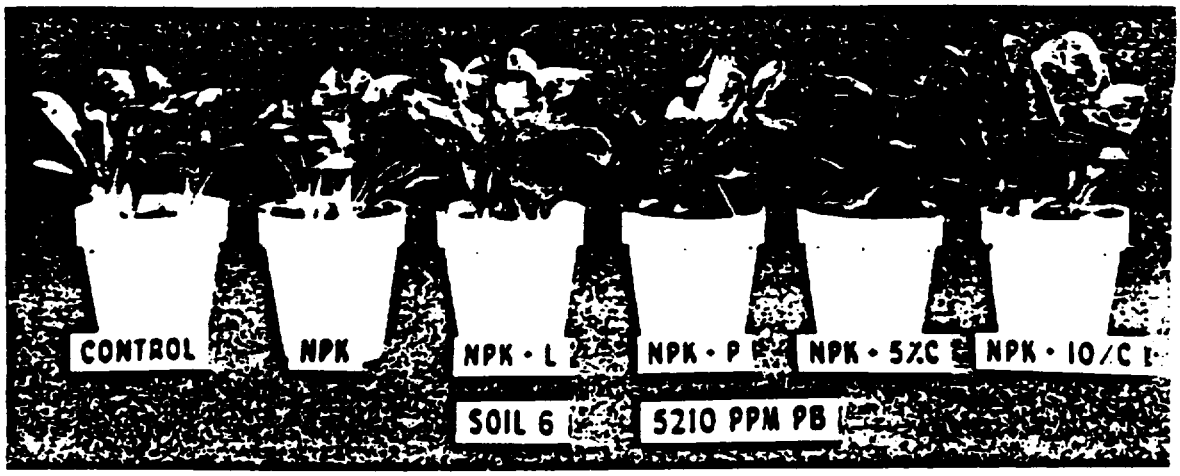


Figure 2 *Plants growing in an urban soil containing 5,210 ppm Pb. The two plants on the right, amended with 5% sewerage sludge compost, grew significantly better than the controls and other treatments.*

Table 1 Number of Fischer 344 rats in each group.

Feeding variables	Soil amendments Null	5% W	10% W	X	Y	Z
Feed alone	6					
+5% (fiber) or 5% sludge	(6)	6	6	6	6	6
+5% control soil (~10 ppm Pb)	6	6	6			
+5% urban soil (~750 ppm Pb)	6	6	6			
+5% urban soil (~1,300 ppm Pb)	6	6	6	6	6	6

Treatments needed to assess the bioavailability of sewage sludge Pb and the effect of sewage sludge amendments on the bioavailability of Pb in contaminated urban soils. Sludges W, X, Y, and Z would have different chemical properties to test the relative importance of sludge iron oxides, organic matter, and limestone in reducing soil Pb bioavailability.

257) processed municipal sewage sludge to Pb contaminated urban soils has been considered by researchers for several years.

Amendment in place is desired compared to removal and replacement of soil, for both reasons of cost and because it may generate Pb-rich dusts which would increase risk of exposure of children. Composted sewage sludge adds large amounts of organic matter, phosphates, and hydrous Fe oxides (all of which can strongly adsorb soil Pb) and would be expected to reduce the bioavailability of Pb in the amended soil.

Early studies of sewage sludge as an amendment for urban soils were conducted at the USDA (Sterret *et al.*, 1991 in press) and included an urban soil measuring 5,210 ppm Pb and 2,620 ppm Zn, and a pH of 6.07. One of the treatments was an amendment with 5% and 10% sewage sludge compost. The plants growing in sludge treated soils, as shown in Figure 2, grew significantly better than controls and the other treatments. Sewage sludge amendments may ameliorate the urban soil Pb problem because they bind Pb which in turn increases the effective particle size of Pb. Also, the amendment would counteract Zn phytotoxicity and enhance plant growth; this should decrease the physical bioavailability of Pb dust from contaminated soils.

Whether or not soil amendments could be used to reduce the bioavailability of soil Pb requires further investigation. Table 1 shows a project design that would test the effect that amendments would have on Pb bioavailability of urban soils.

The possibility of using a soil amendment for solving the Pb problem would be attractive to many municipalities. This action might substantially reduce the need for removing and replacing Pb contaminated inner-city soils. Whatever action is taken, the primary concern is improving the health of children.

Conclusions

Quantity of Pb alone does not define bioavailability. Several physical and chemical properties that influence bioavailability of soil Pb have been described. The two major historical sources of Pb are lead-based paint and leaded gasoline. In terms of particle size, lead-based paint is a potential hazard when it is a coating and it becomes an actual hazard when it deteriorates or is removed, especially by sanding and burning. The combustion of leaded gasoline emitted small particles of Pb dust that accumulates in soils to form an actual hazard, especially within the inner-city.

Zinc also accumulates in urban soil. Zinc is phytotoxic in urban soils when the soil is strongly acid (pH less than 5.4) and Zn quantities are above 1,500 ppm. Physiologically, there are many conditions that lower gastrointestinal tract pH and increase transit time for absorption and retention of Pb. At least nine physical or physiological barriers exist in the gut and tend to decrease Pb bioavailability. Preventing nutritional deficiencies in calcium and iron will reduce bioavailability of soil Pb. Another way to decrease Pb bioavailability would be to amend urban soils with Pb binding agents and plant promoting substances. High quality sewage sludge may serve that purpose. Research is needed to check the safety and feasibility of this amelioration approach.

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The Bioavailability of Lead in Mining Wastes: Physical/Chemical Considerations

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Abstract

In this paper we review the physiological and geochemical factors affecting lead bioavailability, and particularly, the unique physical/chemical properties of lead derived from mining wastes based on both theory and empirical observations. The relationship between blood lead levels and soil lead concentrations derived from epidemiological studies indicates that lead in soil from mining sites appears to have less of an effect on blood lead levels in children than does lead at urban sites or sites with an active lead smelter. Differences in bioavailability of various lead species offers a plausible explanation for the relative differences in their impact on blood lead. In this paper, we evaluate from a physiological viewpoint aqueous solubility, absorption/desorption processes, and uptake mechanisms that may control lead bioavailability within the GI tract. A number of these processes, including the role of passive diffusion, competition with calcium for a common transport mechanism, and the role of organic ligands, are discussed. Geochemical processes that relate to lead bioavailability in the GI tract are also considered. Galena (PbS) and its alteration product, anglesite ($PbSO_4$), are the primary forms of lead associated with mining wastes. Equilibrium thermodynamics and dissolution kinetics of $PbSO_4$ are modeled because this solid is likely to control the concentration of dissolved lead from many mine wastes in the GI tract. The geochemical models DIASTAB and MINTEAQ2 are used to calculate theoretical estimates of lead dissolution and a model is proposed to evaluate lead bioavailability by laboratory methods taking into account both kinetic and equilibrium considerations. This type of model requires calibration with animal toxicological studies of lead bioavailability and with epidemiological studies of different types of lead sites. Ultimately, such a geochemical model could be used to evaluate the potential for public health impacts from a particular type of lead in soil.

Introduction

Children living in communities with elevated soil lead concentrations frequently have higher than average blood lead levels. Although it is generally believed that ingestion of housedust or soil represents an important exposure pathway, the correlation between observed blood lead concentrations and soil lead concentrations among studies has revealed conflicting results (Elwood, 1986). Epidemiological studies of children residing in communities contaminated by lead from smelter or urban sources frequently have higher blood lead levels than children living in areas contaminated with lead from mining wastes, even when soil lead concentrations are similar (Steele *et al.*, 1990). Differences in the source and speciation of lead characteristic of these sources rather than the total amount of lead appear to account for this discrepancy.

Quantifying a physiological response from exposure to lead in soils is often achieved by calculating a blood lead/soil lead slope factor. The slope factor is the ratio of the expected increase in blood lead levels (µg lead per dL blood) to the increase in soil lead concentration, usually in multiples of 1000 µg lead per gram of soil. Studies relating blood lead/soil lead relationships have found that the slopes for children in smelter and urban areas range from 1.1 to 7.6 µg dL^{-1}/1000 ppm, while the slopes for children in mining areas range from 0 to 4.8 µg dL^{-1}/1000 ppm (Steele *et al.*, 1990). These results suggest that lead in soil contaminated from mining activities is less bioavailable than lead in soil derived from urban and smelting sources.

Bioavailability of lead refers to the fraction of ingested lead that is absorbed or taken up physiologically by an individual. Adults absorb roughly 10% of the total amount of lead ingested in the diet (Barltrop and Khoo, 1975; Heard and Chamberlain, 1982), although other studies suggest that absorption may be as high as 15 - 20% (Duggan, 1983). On the other hand, in infants less than 2 years old, 42% of dietary lead was absorbed with intakes =5 µg Pb/kg bodyweight (bw) (Ziegler *et al.*, 1978). Another study estimated up to 53% dietary lead absorption in children 2 months to 8 years with intakes =10 µg Pb/kg bw (Alexander *et al.*, 1973). However, the level of lead absorption through the gastrointestinal tract from soils may be quite different.

Three possibilities may explain the observed differences in lead bioavailability: the size of the lead-containing particle,

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the type or species of lead in soil, and the geochemical matrix incorporating the lead species.

This presentation reviews some of the factors affecting bioavailability of lead in soils and particularly examines the unique physical/chemical properties of lead derived from mining wastes based on both theory and empirical observations. These factors, when excluding differences in exposure, may account for the observed differences in blood lead/soil lead slope factors. The unique characteristics of lead in mining wastes suggest specific means to characterize the bioavailability of these compounds without requiring a blood lead study. We discuss a model that could be used to reproduce laboratory soil extraction results based on a methodology used to test *in vitro* iron availability (Miller and Schricker, 1982) that take into account both kinetic and equilibrium considerations. Such a model could be of use in identifying the potential for public health impacts of a particular type of lead in soil.

Factors Controlling Lead Absorption

Host factors

Physiological factors responsible for absorption and partitioning of chemical forms of lead in the human body may contribute to overall lead bioavailability and explain differences in lead uptake in different subpopulations.

Age and nutrition are the principal host factors that have been studied as determinants of bioavailability. Adults are estimated to absorb 10-15% of lead that is co-ingested with food or water, while infants and children are believed to absorb 50% (ATSDR, 1988). The processes responsible for this difference are not yet known, but differences in metabolic rate, calcium homeostasis and physical development are thought to be important (Chaney *et al.*, 1989).

The influence of diet is illustrated by the observation that absorption can be as high as 70% in adults under fasting conditions due to the very low pH of the stomach under such conditions (Heard and Chamberlain, 1982). Conversely, simultaneous ingestion of lead and food causes reduced absorption *via* neutralization of stomach acid by food contents and reduced acid secretion. James *et al.* (1985) report that the meal effect on lead absorption is a function of pH that lasts about 2-3 hours, the time during which the digesta remains in the stomach under low pH conditions. Increased lead absorption has been correlated with dietary deficiencies of calcium, iron, seen mostly in inner-city children (Mahaffey *et al.*, 1980 and 1986), and with phosphorus, although the latter is an uncommon problem in western societies (Chaney *et al.*, 1989).

The existence of, as yet, unidentified host factors is suggested by the observation of as much as five-fold interindividual variability among adults in the amount of lead absorbed from various foods and beverages (Sherlock, 1987).

Mechanisms of uptake from the gut

Over the last several decades, feeding studies in humans and laboratory animals indicate that solubility, speciation, particle size and host factors such as age and nutrition are all important determinants of lead uptake from the gastrointestinal tract. However, the cellular and molecular mechanisms underlying these observations are poorly understood. In the sections below, we discuss how research pertaining to solubility, particle size and host factors has been incorporated into mechanistic models.

Characteristics of lead that affect uptake The impo lead solubility in determining uptake is demonstrated b that lead in beverages is absorbed twice as readily a food (Ministry of Agriculture, Fisheries, and Food, portion of the lead in food is complexed to soluble ligs amino, carboxylate, and chloride), but the rema associated with a less soluble fraction (*e.g.*, phosphates, and protein complexes). The portion soluble ligands is thought to be more bioavailable fraction associated with sulfides, phosphates, o complexes.

While aqueous solubility is an important factor c lead bioavailability, other factors such as adsorp desorptive processes in the gastrointestinal (GI) tract be significant. These involve interactions between le food contents of the GI tract, as well as partitioning aqueous and lipid compartments within the intest Because of the complexity of the absorption m experimental and theoretical models of the human G incorporate microscale differences in chem physiological conditions are likely to result in mor predictions of lead uptake from the gut than simple estimates.

The role of particle size in bioavailability has be in the context of lead uptake from metallic lead and compounds (Barltrop and Meek, 1979). An inverse re was found between particle size and lead absor relationship was most marked in the 0 to 100 Fundamentally, two properties of lead in small pa recognized: 1) lead in small particles is more easily than lead existing in large particles due to increased s (Healy *et al.*, 1982); and 2) small particles are mor traverse the gastric mucosa and be more efficiently Depending upon the source, small particles may al more lead per unit mass than large particles. This is t smelter-derived particles where lead concentration with decreased particle size (Dorn *et al.*, 1976; Ran 1975). However, mining waste particles tend to ha lead content independent of size (Drexler, 1990 communication), resulting in decreased bioavailabil to smelter-derived material, for a given particle s lead-containing particles are present in food, physi caused by interactions with food and by digestive make it difficult, if not impossible, to predict *in v* size.

Absorption models

One mechanistic model that has been proposed for from the gut is based on linear diffusion of lead ion gastrointestinal mucosa (Karmakar and Jayaraman, gastrointestinal mucosa is treated as a two-pha consisting of an extracellular phase and a cellular p time dependence of lead concentrations in both predicted by the model. With the assumption that lead across the mucosal membrane occurs mainly diffusion accompanied by transport of water, the s

Table 1 *Mineralogy of two mining area soils.*

Lead-bearing phase	Soil 1[a]	Soil 2
Anglesite [$PbSO_4$]	83%	53%
Galena [PbS]	15%	24%
Barite [$(Pb\text{-}Ba)SO_4$]		5%
Lead-phosphates [$Pb_x(PO_4)_y$]		4%
Thorium-lead phosphate [$(Th\text{-}Pb)PO_4$		4%
Plumboferrite [$PbFe_3O_7$]		4%
Plumbojarosite [$PbFe_6(SO_4)_4(OH)_{12}$]		3%
Lead-oxide [PbO]		3%
Native lead [Pb]	1%	
Tin-lead oxide [$SnPbO_3$]	1%	
Total point counts[b]	105	88

[a] both soils originate from Butte, MT

[b] each point counts represents a combination of particle size and number of particles counted in the following manner:

Particle size	Points
1-2 μm	1
2-5 μm	2
5-9 μm	5
10 μm	10
20 μm	20

and continuing in increments of 10 pt. counts/10 μm.

able to calculate the intestinal membrane permeability and the time after ingestion required to reach steady state absorption. The authors found that a steady-state was reached in approximately 19.5 minutes using a lead molecule permeability estimate of $3.34.10^{-3}$ s^{-1} through the intestinal membrane. It should be noted that GI tract chemistry may result in the formation of unionized lead species, *e.g.*, $PbCl_2$ (lead chloride) or $Pb(OH)_2$ (lead hydroxide) for which permeability may be significantly different.

Host factor research has also provided the basis for alternative mechanistic models involving calcium transport and vitamin D metabolism. Such models also provide an explanation for differences in lead absorption between children and adults because calcium uptake decreases with age (Heaney *et al.*, 1975). The simplest model is based on the proposition that lead and calcium compete directly for a common transport mechanism in the gastrointestinal mucosa. Intestinal calbindin proteins, which are normally responsible for transport of calcium across the intestinal mucosa, bind lead with greater affinities than calcium (Fullmer *et al.*, 1985).

However, recent experimental findings (Fullmer and Rosen, 1990) indicate that lead's interactions with calcium, and hence its uptake, are likely more complex. Chicks were maintained on calcium-deficient (0.05%) or adequate (1.2%) diets and fed varying amounts of lead. Consistent with previous studies, the low calcium diet resulted in increased lead uptake. However, concomitant changes observed in three markers of cholecalciferol (vitamin D) action indicate that this was not solely due to direct competition between lead and calcium. In chicks fed the calcium-deficient diet, lead inhibited Ca^{47}

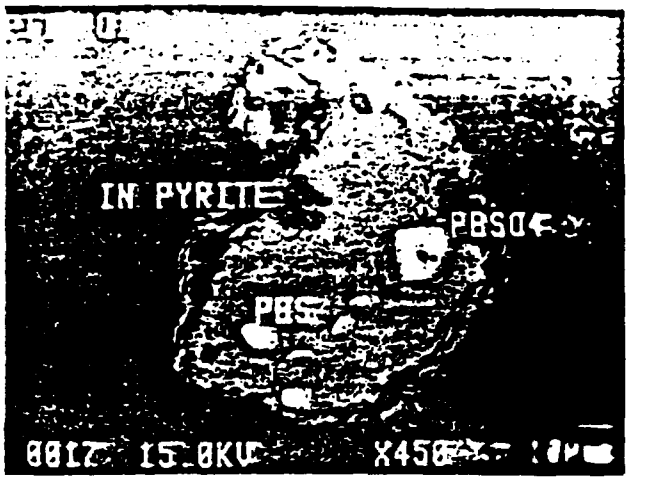

Figure 1 *Photomicrograph demonstrating the [illegible] of primary galena by pyrite*

uptake, calbindin D_{28k} synthesis and alkaline [illegible] activity in a dose-dependent manner. However, [illegible] calcium-adequate diet, lead had no such effect [illegible] levels, it actually increased all three markers [illegible] comprehensive, unifying model has not been [illegible] elaborated to explain these results, they do point [illegible] important interactions between lead and the [illegible] endocrine system.

Chaney *et al.* (1988) propose a novel [illegible] explanation for the inverse relationship between [illegible] on the one hand, and dietary calcium and phosphorus [illegible] other. Drawing an analogy to the zinc deficiency disease, Acrodermatitis Enteropathica, they suggest that lead coprecipitates with calcium phosphates formed during digestion and that such lead coprecipitates are poorly or not absorbed at all. This coprecipitation occurs only when calcium and phosphate are present at high concentrations in the digesta. Passage of the digesta from the low pH of the stomach to the higher pH's of the small intestine and the duodenum is thought to provide optimal conditions for the coprecipitation to occur. When calcium and/or phosphorus are present at low concentrations, coprecipitation does not occur and uptake of lead is unaffected.

It should be noted that the Integrated Uptake/Biokinetic (IU/BK) model, developed to describe the effects of environmental lead on community blood lead levels in young children (Harley and Kneip, 1985), assumes a nearly linear dose-response relationship between soil lead and blood lead, but tends to overpredict blood lead above 30 μg dL^{-1} (USEPA, 1989). At these higher levels, a saturation of uptake mechanisms appears to occur. Environmental blood lead studies indicate a decreasing dose-response relationship over increasing soil lead concentrations (Bornschein *et al.*, 1988, 1989). The decreasing blood lead slope with higher soil lead concentrations would suggest that the bioavailability of lead decreases at increasing concentrations of lead in soil.

Figure 2 *Photomicrograph of mine tailings demonstrating the authogenic reaction of galena (interior of crystal) to anglesite (rind)*

Effect of organic ligands on lead absorption

The presence of organic ligands, their ability to complex lead, and the stability of the complexes formed may affect both solubility and absorption of lead in the small intestine. The ingestion and subsequent decomposition of food substances in the gastro-intestinal tract will release organic ligands, including organic acids, *e.g.*, acetate, ascorbate, citrate, lactate, and amino acids from protein degradation (Tortora, 1980, Marty and Raynaud, 1966). The dissolution of lead from a lead-bearing mineral in the stomach results primarily in $PbCl^+$ due to the high concentration of chloride and the common-ion effect (Healy, 1984). However, as the digestate enters the duodenum, the pH is raised to approximately 6.5. The subsequent degradation of ingested material generates organic ligands that compete with chloride for complexation of Pb^{2+} throughout the small intestinal environment. The stability constants of amino and organic acid complexes with Pb^{2+} which have been measured at neutral pH and 0.1 ionic strengths indicate that Pb-ligand complex stability follows the order, cysteine > citrate > tyrosine > acetate > ascorbate (Martell and Smith, 1974 and 1977). However the effects of such complexation on lead absorption have not been studied.

Studies on uptake of iron indicate that formation of soluble, uncharged complexes may enhance uptake of metals from the gastro-intestinal tract (Van Campen, 1973). For example, histidine, lysine, and cysteine have been shown to enhance iron uptake in the duodenum of Sprague-Dewley rats, due to the formation of complexes sufficiently stable to maintain the solubility of ferric iron. In addition, passive diffusion of neutral lead species across the intestinal epithelium is enhanced by the absorption of water (Blair *et al.*, 1979, Healy, 1984, and Karmakar and Jayaraman, 1988). Thus the formation of stable, soluble Pb-organic ligand complexes may enhance absorption of lead, due to passive diffusion or reduced interaction between ionized lead and tissue phosphate ions (Blair *et al.*, 1979).

Review of lead mineralogy

In ore deposits, lead occurs only in one valence state (II) in a mineralogical form generally restricted to galena PbS associated with pyrite in porphyry, volcanic massive sulfide and stratiform and strata-bound deposits (Figure 1 Evans 1980). Upon exposure of the primary ore to surface conditions a wide variety of secondary (alteration) products may form including oxides (PbO, PbO_2), carbonates ($PbCO_3$), and sulfates ($PbSO_4$). These alteration products generally form oxidation-reaction products that coat the primary sulfide (Figure 2). Consequently, because of reactions at the mineral surface, simply specifying that a lead-bearing mine waste contains galena in the mineral assemblage is an inadequate representation of the material.

Lead associated with mining waste consists primarily of galena (PbS) altered to anglesite ($PbSO_4$) in the surficial horizons of waste piles (Tetra Tech, 1985, CDM 1989). Lead sulfates ($PbSO_4$) and oxides (PbO, PbO_2) are the predominant forms of lead at smelter sites (Foster and Lott 1980). Lead associated with mining activities is typically found in complex lead-bearing solids, in which lead substitutes for other metals in the crystal lattice, in addition to the common carbonates and sulfates (Table 1). The major forms of lead present at a mine site appear to be source-specific, in that the spatial variability is more pronounced between sources than between areas at one site (CDM, 1989, Tetra Tech, 1985). Phases may be best identified using an electron microprobe with energy dispersive phase stoichiometry. The resulting spectra are used to identify the phases present.

Foster and Lott (1980) studied the composition of lead compounds in airborne particulates associated with ore handling, sintering, and blast furnace operations around a lead smelter in Missouri. Lead sulfide (PbS) was observed as a major constituent in samples associated with ore handling while lead sulfate ($PbSO_4$) and a lead oxide species ($PbO.PbSO_4$ (lead sulfate, basic)) appeared to be the dominant species associated with smelting operations possibly due to fugitive lead emissions from the stack.

It should be recognized that lead contamination in soil from historical mining and smelting sites may be due in part to lead derived from gasoline and lead from house paints. Until 19 lead was added to gasoline as both tetramethyl and tetraethyllead as an antiknock agent (NAS, 1979). Several investigations have demonstrated that lead concentrations are elevated adjacent to highways, with concentrations decreasing exponentially, both with soil depth and distance away from the road (Motto *et al.*, 1970, Lagerwerff and Specht, 19 Following the phaseout of high concentrations of lead in gasoline (1974-1980), lead concentrations have decreased in soils near highways (Byrd *et al.*, 1983). The major form of lead in automobile exhaust is PbClBr (Chaney *et al.*, 1989), which is rapidly transformed to sulfates and carbonates in the environment (Biggins and Harrison, 1980).

Weathering of lead paints can also contribute to lead in soil around the exterior walls of houses (Chaney *et al.*, 19 due to the use of lead in the octoate, oxide, carbonate, sulfate and chromate forms as pigments in paints. Although current regulations limit the addition of lead to 0.06 percent (

Table 2 *Lead-bearing mineral forms identified in text.*

Formula	Name
$PbCl_2$	Lead chloride, or cotunnite
$Pb(OH)_2$	Lead hydroxide, or lead hydrate
PbS	Lead sulfide, or galena
PbO	Lead oxide, or massicot, or litharge
PbO_2	Lead dioxide, or plattnerite
$PbCO_3$	Lead carbonate, or cerrussite
$PbSO_4$	Lead sulfate, or anglesite
$PbSO_4$. PbO	Lead sulfate, basic, or lanarkite
$Pb_5(PO_4)_3Cl$	Pyromorphite
$Pb_3(PO_4)_2$	Lead phosphate

1979), surfaces coated with paint prior to 1950 and soil impregnated with lead containing paint chips are a potential source of lead contamination.

Particle size of lead phases at mining and smelting sites

Technologies used to extract and process lead have changed significantly over the last century. Techniques used over time to mechanically and chemically extract lead have resulted in a variety of types and forms of lead in the environment. Valuable minerals, including lead, are commonly separated from gangue or waste rock by one of two methods. Both methods involve a crushing or grinding step, followed by differing methods of concentration or beneficiation. Before the twentieth century, the technique used to concentrate lead minerals from waste rock depended on gravity, taking advantage of the higher density of the mineral particles. For example, galena (PbS) has a density of 7.6 g cm^{-3} compared to a typical waste rock which has a density of 2.7 g cm^{-3} (Davies, 1983). The waste rock or spoils from this type of ore beneficiation process is known as chat.

In 1906, the process of froth flotation was patented (Davies, 1983). The process is based on differences in the physicochemical surface properties of mineral particles and waste rock. In froth flotation, the ore must first be finely ground (usually to about 200 µm) to liberate the mineral component of the ore from the waste rock. The finely ground ore is then mixed with water containing a frothing or foaming agent which selectively coats the surface of the mineral particles and makes them hydrophobic. When air is bubbled through the mixture, the coated mineral particles rise to the top in a froth and are separated from the waste rock, which sinks to the bottom (Aplan, 1985). The waste rock produced from froth flotation is known as tailings, which are typically smaller in particle size and lower in residual metals compared to chat. Spoils piles in the Old Lead Belt area of Missouri averaged 2,000-4,500 µg g^{-1} Pb, while those in the New Lead Belt area where froth flotation was used more extensively averaged only 300 µg g^{-1} Pb (Wixson *et al.*, 1984).

Mining and milling processes usually generate relatively large particles. The particle size of tailings from different ores have been measured in the range of 10 to 1000 µm, typically with none smaller than 1 µm (Andrews, 1975). In a sample of chat from lead ore, only 14% of the particles were smaller than 100 µm (Lagerwerff and Brower, 1975). At the Sharon

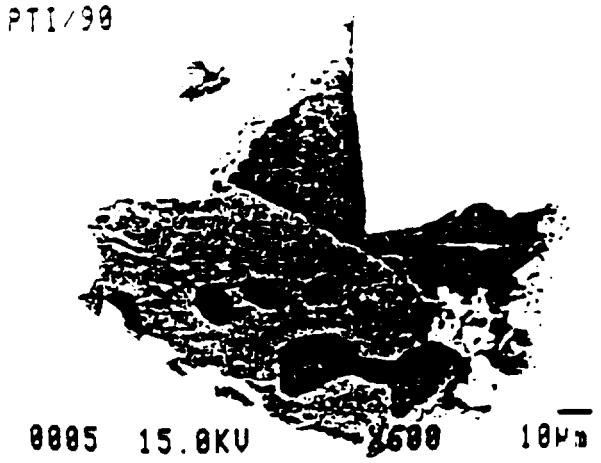

Figure 3 *Photomicrograph showing primary galena encapsulated by pyrite altering to $FeSO_4$.*

Steel/Midvale Tailings site in Utah, active from 1910 to 1971, mineral distribution and particle size characteristics of tailings piles were determined as part of a comprehensive study to evaluate the feasibility of reprocessing mine tailings to recover lead and other minerals. Lead sulfide (PbS) particle sizes resulting from liberation in laboratory sample preparation, generally ranged from less than 10 to 230 µm with a typical range of 30 - 60 µm (Hazen Research Inc., 1989).

The particle size as well as the mineralogy of lead derived from smelter emissions is quite different from lead derived from mining/milling operations (Table 3). Lead particles released through smelter stacks are typically less than a few microns in diameter. A study of smelters in Missouri reported that 66 percent of the mass of lead measured in the air on a farm near a smelter (800 m from the smelter stack) was associated with particles smaller than 4.7 µm as described in U.S. EPA (1986a). In Meza Valley, Yugoslavia, a series of studies investigated lead exposures from a mine and a smelter.The mean particle size of stack emitted lead-bearing particles measured during a 24 hour sampling event was less than 0.8 µm (U.S. EPA, 1986b). Particle size characteristics and associated forms of lead in soils in this area were, however, not described.

Thermodynamics and equilibrium dissolution theory

Thermodynamic constraints may be used to predict aqueous lead concentrations in equilibrium with a solid lead phase (Garrels and Christ, 1965, Lindsay, 1979) that can be applied to estimate solubilities of lead in the GI tract. However, it should also be noted that such models do not consider the time available for dissolution, which may preclude attaining equilibrium solubility. The thermodynamic approach forms the basis for geochemical computer codes that are used to solve complex speciation problems involving hundreds of aqueous complexes and several mineral phases. Computer codes such as DIASTAB (B. Robbins, January 1988, personal

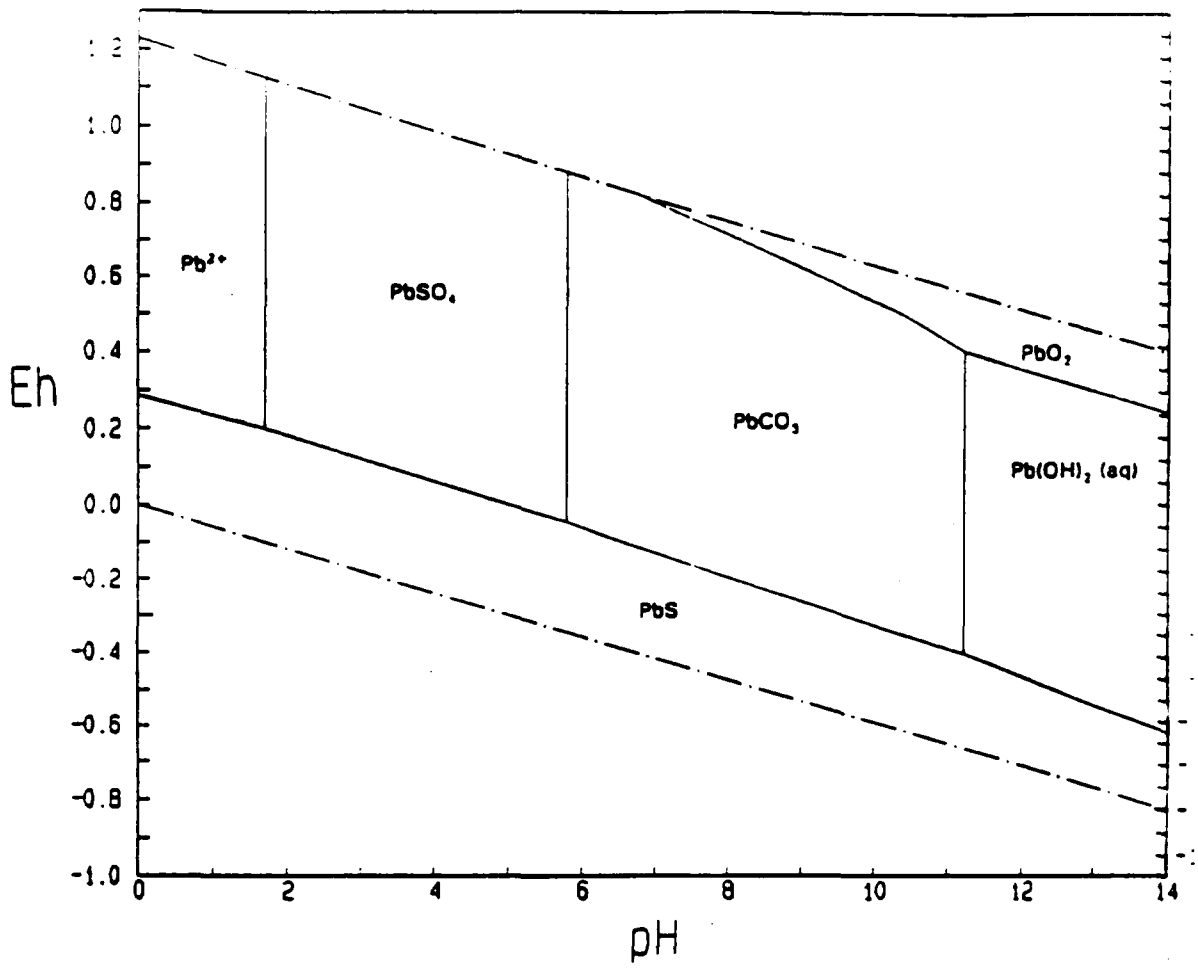

Figure 4 *Eh-pH diagram of Pb.* $\Sigma Pb = 10^{-4}$ *M,* $\Sigma S = 10^{-4}$ *M,* $\Sigma Cl = 10^{-4}$ *M,* $\Sigma C = 10^{-3.5}$.

communication) and SOLUPLOT (Bethke, 1978) provide Eh-pH, solubility, and distribution diagrams (Figures 4 and 5) from free energy data, while the code MINTEQ (Felmy *et al.*, 1983) and subsequent generations, *e.g.*, MINTEQA2 predict total aqueous metal concentrations at specified values of Eh, pH, and reactant concentrations. Speciation codes are also used to determine the major metal complexes in solution *i.e.*, the distribution of lead species (Pb^{2+}, $PbCl^{+}$, and $PbCl_2$ (in the presence of chloride)).

Theoretical solubility of lead in the gastrointestinal tract

Use of geochemical models to estimate lead solubility in the GI tract after ingestion requires knowledge of the frequency of the predominant lead-bearing phases in a soil or mining waste sample. Mineral stoichiometries are identified from the solid phase microprobe spectra. Thermodynamic data (free energy of formation) are available in the literature for many of the common solids. If unavailable, free energy may be estimated by determining the ratios of the end member compounds and proportioning the free energy accordingly (Tardy a 1976; Nordstrom and Munoz, 1985). Estimation of e solubility can only be employed for those solids identifiable structure and for which reliable therm data has either been published or may be estimated.

Solubility of a lead-bearing phase is a function c strength and composition of the solution, the degree lead complexing, and the Eh, pH, and temperat environment. To illustrate the dissolution of a solid tract, consider a pure, euhedral, galena crystal, r surficial mine waste, that undergoes oxidation, form of anglesite (PbSO4) around a galena core. This reaction is observed routinely in photomicrographs waste (Figure 2) and may be represented by the redo

$$PbS + 4H_2O \rightleftharpoons PbSO_4 + 8H^{+} + 8e^{-}$$

Typically galena is not stable at surface temp pressure unless encapsulated within pyrite or the pyr product, $FeSO_4(s)$ (Figure 3). Thus, the pertine

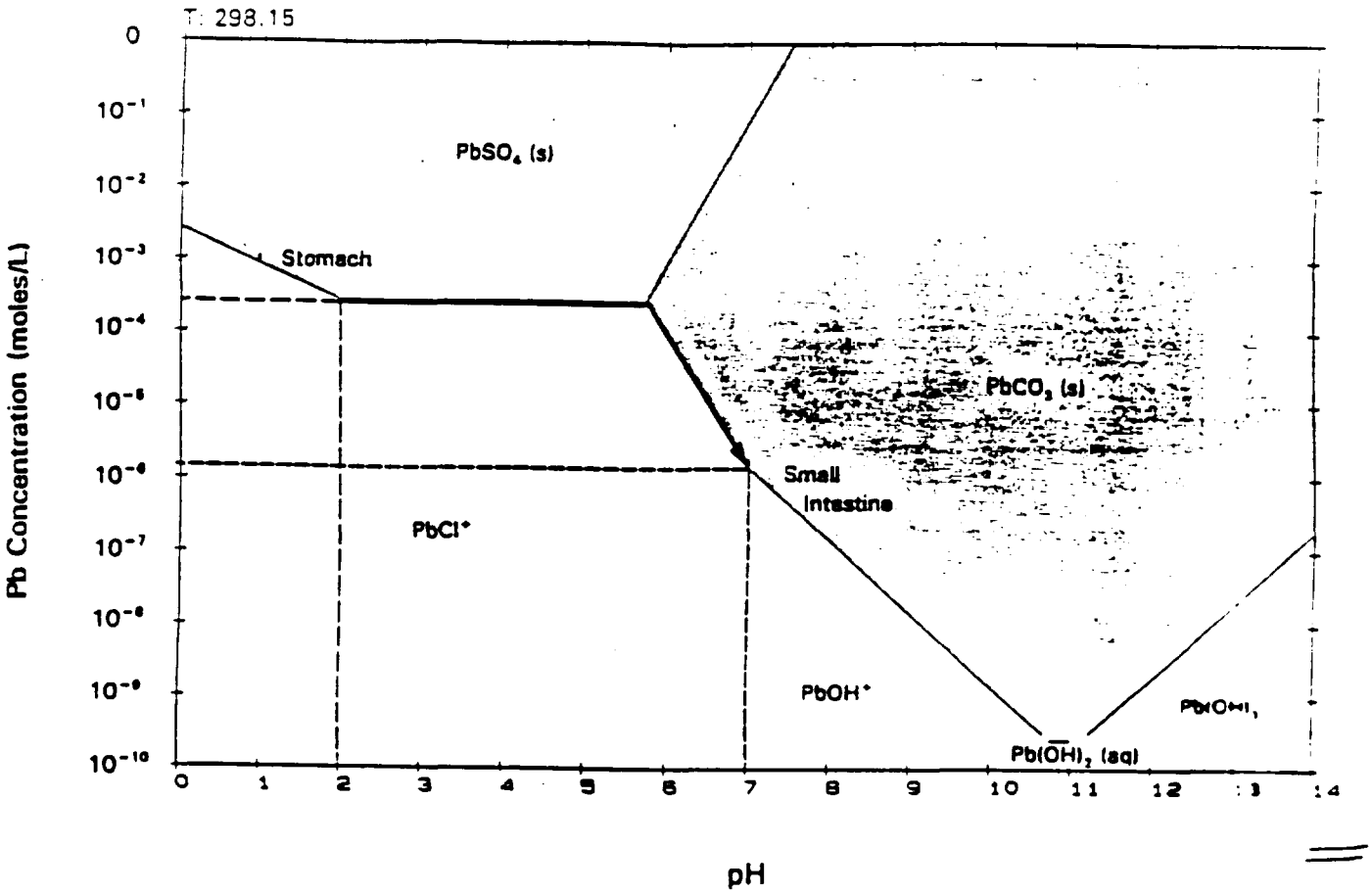

Figure 5 *Solubility of $PbSO_4$ (s) and $PbCO_3$ (s) in equilibrium with pure water containing $\Sigma Cl = 10^{-2}$ M Shading denotes solid stability field.*

describing dissolution of ingested $PbSO_4$ in a solution consisting primarily of HCl in the stomach may be described by:

$$PbSO_4(s) + HCl \rightleftharpoons Pb^{2+} + Cl^- + HSO^{4-} \quad (2)$$

Using the thermodynamic data for $PbCl_n^{2-n}$ complexes and the products and reactants of equation (2), (Table 4), the principal inorganic lead complexes resulting from equilibrium dissolution of $PbSO_4$ can be evaluated using the equilibrium speciation computer models described earlier.

Application of geochemical models: The currently accepted model for dissolution of lead from ingested soils assumes solubilization of the lead-bearing phases in the human stomach at a pH of 1 to 2 (Miller and Schricker, 1982; Chaney *et al.*, 1989) with a residence time of 2 to 3 hours (Malagaleda *et al.*, 1977). Neutralization of the solution by bicarbonate ion occurs as the bolus passes from the stomach into the small intestine and the pH increases to 6-7 (Miller and Schricker, 1982). This condition results in a net negative surface charge on solid surfaces to which positively charged lead species (*e.g.*, Pb^{2+}, $PbOH^+$, $PbCl^+$) sorb. Consequently, dissolved lead concentrations may decrease as the pH increases from the stomach to the small intestine, assuming that adsorption to surfaces rather than complexation by soluble ligands is controlling Pb solubility. MINTEQA2 is capable of modeling sorption of cations to soil surfaces; however, due to the absence of pertinent data, *i.e.*, the specific surface area of the sorbent, the net point of zero charge of the solid, and the concentration of cations competing for sorption sites, modeling of sorption to soil surfaces was not attempted at this time.

Examination of the Eh-pH diagram (Figure 4), constructed using DIASTAB, indicates that $PbSO_4$ and $PbCO_3$ will control lead solubility under geologic conditions below and above pH 6, respectively, under oxidizing conditions if both sulfate and carbonate are present in sufficient concentrations to allow precipitation. Under reducing conditions, PbS controls lead solubility; however, experimental Eh data obtained using New Zealand White rabbits (Davis *et al.*, in press) indicates that oxidizing conditions prevail in both the stomach and small intestine.

The anglesite and cerrusite solubility diagram (Figure 5)

Table 3 *Properties of lead emitted from different sources.*

Source	Predominant particle size	Dominant species
Mining/milling site	10 to 1,000 μm	PbS, $PbSO_4$, $PbCO_3$
Smelting site	<1 - 5 μm	PbO, PbO·$PbSO_4$

Table 4 *Thermodynamic database for geochemical modeling.*

Lead species	ΔGf kcal	ΔHf kcal	Ref.
Aqueous			
Pb^{+2}	-5.83	-0.41	1
$PbOH^+$	-54.09		1
$Pb(OH)_2(aq)$	-96.10		2
$Pb(OH)_3^-$	-137.57		1
$PbCl^+$	-39.39		1
$PbCl_2(aq)$	-71.03		1
$PbCl_3^-$	-101.89		1
$Pb(HS)_3^-$	-19.8		3
$Pb(HS)_2(aq)$	-20.9		3
$PbSO_4(aq)$	-187.20		1
Solids			
$PbCl_2(s)$ cotunnite	-75.07	-85.90	1
$Pb(OH)_2(s)$	-108.08	-123.0	1
PbClOH(s) laurionite	-93.50		1
PbClOH(s) laurionite	-114.8		3
PbS(s) galena	-23.59	-24.00	1
PbO(s) litharge	-45.15	-52.34	1
PbO(s) massicot	-44.91	-51.94	1
$PbO_2(s)$ plattnerite	-51.94	-66.30	1
$PbSO_4(s)$ anglesite	-194.36	-219.86	1
$PbSO_4.PbO(s)$ lanarkite	-246.70	-280.00	1
$PbCO_3(s)$ cerussite	-149.50	-167.09	1
$PbO.PbCO_3(s)$	-195.20	-219.50	1
$2PbO.PbCO_3(s)$	-241.90	-272.94	4
Other species			
H_2O	-56.67	-68.31	1
S^{-2}	20.5	7.91	1
HS^-	2.89	-4.21	1
$H_2S(aq)$	-6.64	-9.59	1
SO_4-2	-177.94	-217.33	1
HSO_4^-	-180.66	-212.07	1
$CO_2(g)$	-92.26	-94.05	1
CO_3^-	-126.15	-161.83	1
HCO_3^-	-140.25	-165.39	1
$H_2CO_3(aq)$	-148.92	-167.14	1
Cl^-	-31.36	-39.96	1
HCl(aq)	-22.78	-22.06	1
Organic Ligands			
Pb(acetate)	-2.93[a]		5
$Pb(acetate)_2$	-4.77		5
Pb(ascorbate)	-2.41		5
Pb(citrate)	-5.92[b]		5
$Pb(citrate)_2$	-8.29[b]		5
Pb(cysteine)	-15.82		6
Pb(tyrosine)	-5.65[c]		6
$Pb(tyrosine)_2$	-11.65[c]		6

[a]All values for organic ligands are at 25°C and 0.1 ionic strength unless otherwise indicated.
[b]25°C and 2.0 ionic strength.
[c]20°C and 0.37 ionic strength.

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1. Wagman *et al.*, 1982
2. Lind, 1978
3. Naumov *et al.*, 1974
4. Rossini *et al.*, 1952
5. Martell and Smith, 1977
6. Martell and Smith, 1974

constructed using DIASTAB, demonstrates that the ac... Pb^{2+} will be $10^{-3.48}$ (69 mg L^{-1} of dissolved Pb^{2+}... stomach if the bathing solution reached equilibrium ... anglesite at pH 2. However, the lead activity is predic... decrease during passage through the small intestine. ... equilibrium between precipitation of $PbCO_3$ and forma... $PbCl^+$ and $PbOH^+$ will control lead solubility.

The efficacy of MINTEQA2 as a predictive to... investigated in this study by comparing experimental ... model results. The experimental solubility of angle... different solutions has been measured by several author... Dyrssen *et al.* (1969) in 0.2 M sodium perchlorate (62.5 m... and Giordano (1989) in 10^{-3} M acetate at 40C (38 mg L^{-1}... a review of the available data, Clever and Johnston ... recommended an anglesite solubility of 35 mg L^{-1} in w... 35C. Simulations using MINTEQA2 predict 45 mg L... anglesite dissolution in 10^{-3} M acetate ($a_{Pb2+} = 10^{-3.95}$, ... mg L^{-1} in water ($a_{Pb2+} = 10^{-3.88}$) both at 37C. Both these ... compare well with the experimental data.

MINTEQA2 predicts that dissolution of anglesite ... stomach will produce 69 mg L^{-1} of dissolved lead ... $10^{-2.77}$) in solution (Table 5), decreasing to 37 mg ... $10^{-4.12}$) as the digestate passes into the small intestine. ... addition of organic acids capable of complexing ... and citrate at 10^{-4} M) increases dissolved lead to ... mg ... the small intestine, while the addition of 10^{-3} M ... absence of organics) decreases dissolved lead to ... ($a_{Pb2+} = 10^{-4.74}$) due to the precipitation of ... (pyromorphite), $Pb_5(PO_4)_3(OH)$ and ... phosphate). These results indicate that organic ... lead in the small intestine will increase ... solubilized lead while decreasing the activity of ... presence of phosphate ion may cause a decrease in ... lead if kinetic constraints allow the precipitation o... lead-bearing species.

Dissolution of galena (PbS) at pH 2.0 and Eh = ... is predicted to result in 69 mg L^{-1} dissolved lead (a... $10^{-3.77}$) due to precipitation of anglesite, while dissolu... galena at pH 7.0 and Eh = +200mV is predicted to resu... mg L^{-1} ($a_{Pb2+} = 10^{-7.20}$) dissolved lead, control... precipitation of $Pb_4O_3(SO_4)$, $PbSO_4.PbO$, and $PbSO_4$. ... mass of galena was assumed to be present, oth... MINTEQA2 would continue to dissolve galena and prec... anglesite *ad infinitum*. The modeled concentrations are c... to the experimental data of PbS dissolution which resu... 480 mg L^{-1} dissolved lead in *in vivo* gastric fluid (Heal... 1982). The discrepancy between modeled and exper... results at pH 2.0 is probably due to kinetic constraints ... precipitation reactions predicted to control dissolv... concentrations during dissolution of galena.

Dissolution of the minerals massicot (PbO) and c... ($PbCO_3$) were also modeled using MINTEQA2 becau... two forms of lead have been observed at smelting and ... sites. The resulting lead concentrations of $1.4x10^7$ mg ... PbO and $1.6x10^5$ mg L^{-1} for $PbCO_3$ indicate that c... dissolution will occur at pH 2.0 and dissolved lead in ... tract solutions at equilibrium with these minerals will be ... by the mass of material in contact with solution.

MINTEQA2 results for speciation of lead (T... indicate that Pb^{2+} will predominate in the stomach and ... relative concentration of Cl^- in the small intestine will ...

Table 5 *Results from MINTEQA2 analyses.*

Modeled conditions: lead concentrations (mg L^{-1})	Galena PbS	Anglesite $PbSO_4$	Massicot PbO	Cerussite $PbCO_3$
Lead conc. in stomach pH 2.0, 0.01 M Cl^-	69[b] (1.7×10^{-4})[c]	69 (1.7×10^{-4})	1.4×10^{7}[e] (6.5)	1.6×10^{5}[e] (0.32)
Lead conc. in small intestine pH 7.0, 10^{-7} M Cl^-	10[d] (6.3×10^{-8})	37 (1.3×10^{-4})		
Lead conc. in small intestine pH 7.0, organics present[a]		61 (7.6×10^{-5})		
Lead conc. in 10^{-3} M acetate		45 (1.1×10^{-4})		
Lead conc. in small intestine pH 7.0, 10^{-7} M Cl^-, 10^{-3} M Ca^{2+}, 10^{-3} M PO_4^{-3}		7.5[f] (1.8×10^{-5})		

[a]Both acetate and citrate present at 10^{-4} M, 10^{-7} M Cl^-
[b]Due to precipitation of angelsite
[c]Numbers in parentheses indicates free Pb^{2+} ion activity
[d]Due to precipitation of $Pb_4(SO_4)$, lanarkite ($PbSO_4$.PbO), and anglesite
[e]Dissolved lead limited by mass of material in contact with solution
[f]Due to lead-phosphate precipitates discussed in text

the speciation of lead between Pb^{2+}, lead-chlorides, and lead-hydroxides. The addition of two organic ligands to the simulation suggests that these species may be important in controlling lead solubility in the GI tract.

Application of MINTEQA2 to the dissolution of anglesite in water and acetate indicates that the model is capable of replicating the experimental results of simple systems. However, when MINTEQA2 is applied to gastrointestinal chemistry, differences between the limited experimental data and model results are evident. The MINTEQA2 results presented here indicate the relative importance of several common lead-bearing phases, the effects of phosphate and organic ligands, and the speciation of lead as a function of pH and chloride concentration. However, any attempt to accurately model GI chemistry must simultaneously take into account the presence of organics, PO_4^{3-}, HCO_3^-, and sorption phenomena among other variables in the GI tract. Thus, thermodynamic models should be viewed with caution due to uncertainties in

Table 6 *Results from MINTEQA2 analyses.*

Solid phase	Distribution of lead in stomach pH 2.0 0.01 M Cl^-	Distribution of lead in SI pH 7.0 0.1 M Cl^-	Distribution of lead in SI pH 7.0 10^{-7} M Cl^-	Distribution of lead in SI pH 7.0 organics[a]
Galena PbS	72% Pb^{2+} 28% $PbCl^+$	27% Pb^{2+} 64% $PbCl^+$ 6% $PbCl_2$(aq) 3% $PbOH^+$	84% Pb^{2+} 16% $PbOH^+$	29% Pb^{2+} 6% $PbOH^+$ 63% Pb citrate 2% Pb acetate
Anglesite $PbSO_4$	70% Pb^{2+} 26% $PbCl^+$ 4% $PbCl_2$(aq)	27% Pb^{2+} 63% $PbCl^+$ 5% $PbCl_2$(aq) 3% $PbOH^+$ 2% $PbSO_4$(aq)	80% Pb^{2+} 14% $PbOH^+$ 6% $PbSO_4$(aq)	30% Pb^{2+} 5% $PbOH^+$ 4% $PbSO_4$(aq) 59% Pb citrate 2% Pb acetate

[a]Both acetate and citrate present at 10^{-4} M, Cl^- at 10^{-7} M

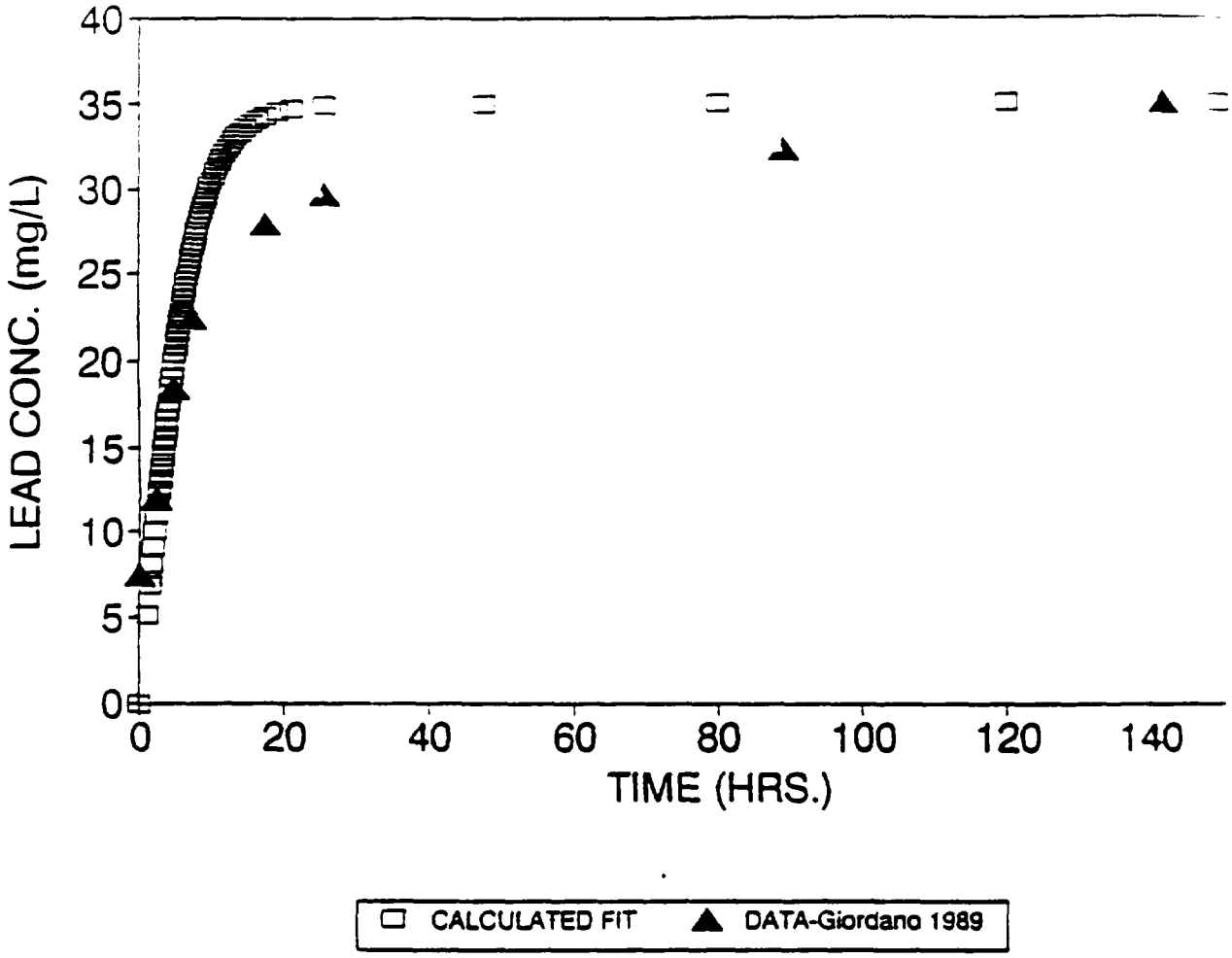

Figure 6 *Runge-Kutta fit to $PbSO_4$ dissolution data*

the input parameters.

Kinetics of Lead Dissolution

To date, no data have been generated that accurately represent the dissolution of anglesite ($PbSO_4$) in the GI tract because the limited residence time of soil in the stomach (2 to 3 hours, Malagaleda *et al.*, 1977) precludes attainment of steady state conditions. As a result, dissolution of lead-bearing phases may be controlled by a kinetic process, rather than by equilibrium thermodynamics. Therefore, the ability to predict the rate of mineral dissolution in the stomach environment is critical in estimating lead bioavailability from mining waste. Anglesite dissolution kinetics were modeled in this paper because this solid is likely to control the concentration of dissolved lead from many mine wastes in the GI tract.

A literature search on the dissolution kinetics of lead-bearing solid phases under physiological conditions indicates no previous work on this topic. However, the time dependence of $PbSO_4$ dissolution in buffered acetate solution has been examined by Giordano (1989), who found that $PbSO_4$ reached equilibrium after approximately 40 hours at 25°C in pH 4.6 buffered acetate solution (Figure 6). By analogy, these data imply that equilibrium between $PbSO_4$ and stomach fluids may not be attained during the residence time of mine wastes in the stomach.

Kinetic models

An alternative to an equilibrium based model to dissolution of $PbSO_4$ in the GI tract is a rate-base description of the system. For example, dissolution of been shown to be dependent on both solubility and par (Healy *et al.*, 1982). These two factors are combine Noyes-Whitney dissolution rate law (Healy, 1984) *i.e.*

$$dC/dt = k\sigma (C_s - C) \qquad (3)$$

where C is the concentration of lead in bulk solution surface area of the particle, C_s is the solubility, ar constant of proportionality. This model predicts that t lead dissolution is proportional to both PbS solubilit surface area of the PbS particles, which is dependen particle size and shape. Therefore, to examine the kir the mechanism of PbS dissolution, the surface are dissolving solid must be relatively constant during t of a dissolution experiment, allowing the rate const normalized for surface area.

Several potential reaction mechanisms fo dissolution in the gastric environment are desc

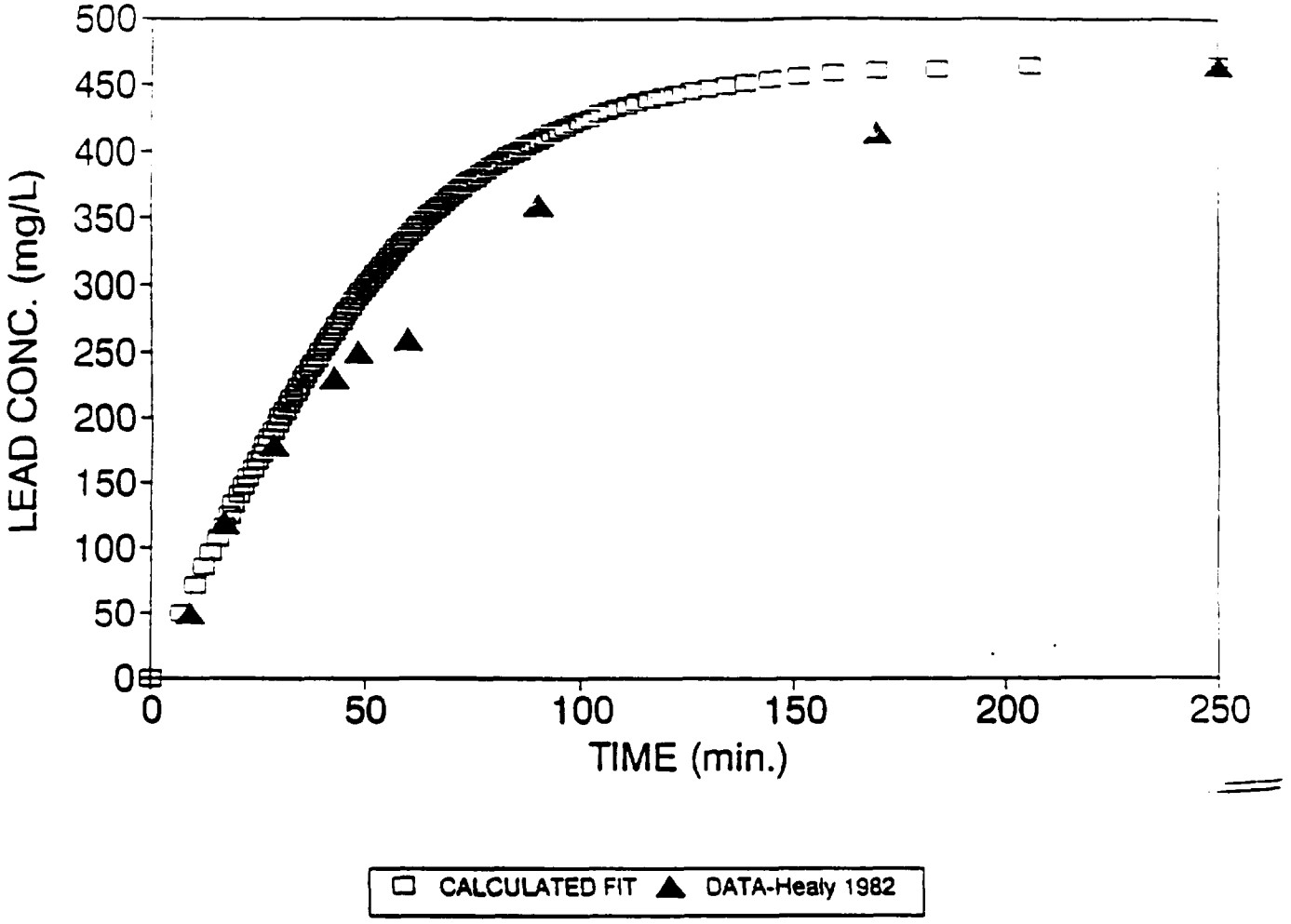

Figure 7 *RungeKutta fit to PbS dissolution data*

equations (4)-(6). Reverse reactions are considered in all of the mechanisms because precipitation of $PbSO_4$ becomes important as the system approaches equilibrium.

Unimolecular:

$$PbSO_4 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Pb^{2+} + SO_4^{2-} \qquad (4)$$

Bimolecular:

$$PbSO_4 + Cl^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} PbCl^+ + SO_4^{2-} \qquad (5)$$

Consecutive second order:

$$H^+ + PbSO_4 \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} Pb^{2+} + HSO_4^- \qquad (6)$$

$$Pb^{2+} + Cl^- \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} PbCl^+$$

The unimolecular reaction mechanism simulates simple $PbSO_4$ dissolution. After rearrangement the equation results in the rate expression:

$$d[Pb^{2+}]/dt = k_1 - k_{-1}[Pb^{2+}]^2 \qquad (7)$$

assuming that $m_{Pb^{2+}} = m_{SO_4^{2-}}$. Equation (7) can be rearranged and integrated to yield an empirical solution that expresses $[Pb^{2+}]$ in terms of time and rate constants. However, the algebraic solution becomes quite complex. To provide an analytical solution to equation (7), the fourth order Runge-Kutta-Fehlberg method (Maron, 1982) was coded in Pascal. As an initial test, the code was evaluated using $PbSO_4$ dissolution data published by Giordano (1989). A forward rate (k_1) was determined from the first three data points and assumed to be constant throughout the experiment. This allows calculation of the backward rate (k_{-1}) at equilibrium when $k_1 = [Pb^{+2}]^2 k_{-1}$. The Runge-Kutta method was then used to predict $[Pb^{2+}]$, based on k_1, k_{-1} and time (Figure 6). The solution to Equation 7 accurately simulates the experimental data at the early time period, when the reaction rate is linear, and also as the reaction reaches equilibrium, but fails to accurately predict $[Pb^{2+}]$ at intermediate times. This discrepancy is probably due to two factors. First, equation (4) fails to take into account subsequent reactions of Pb^{2+} and SO_4^{2-} which may drive the reaction forward, and secondly, there is no attempt to account for the effect of changing particle size on the dissolution rate. Experimentally, this latter variable may be eliminated by

utilizing relatively large particles, resulting in negligible surface variations, (proportional to r^2 for spherical particles) over the course of the experiment. The Runge-Kutta method could not be applied to equations (5) and (6) because experimentally determined chloride and sulfate concentrations in the stomach were not available.

As a second test of the accuracy of the kinetics model, data on PbS dissolution (Healy *et al.*, 1982) (particle size 100 ±20 μm) in *in vivo* gastric fluid were also interpreted using the Runge-Kutta method (Figure 7). This application is appropriate because the first step in dissolution of PbS is analogous to equations (4) and (7), even though Pb^{2+} and S^{2-} will participate in further reactions. The calculated fit follows the experimental data reasonably well, implying that the dissociation of PbS to form Pb^{2+} and S^{2-} may be the rate determining step in dissolution of PbS. However, reaction of S^{2-} with O_2 to form SO_3^{2-}, $S_2O_3^{2-}$, and SO_4^{2-} has been shown to behave according to a first order rate law when O_2 is in excess and proceeds with a rate at pH 4 that is similar to the PbS dissolution reaction (O'Brien and Birkner, 1977). Therefore, the rate of S^{2-} reaction may influence the net conversion of reactants to products.

Consequently, a more sophisticated model is necessary to simulate galena dissolution in the GI tract. Based on MINTEQA2 results, equilibrium distribution of lead at pH 2.0 favors Pb^{2+}, with $PbCl^+$ and $PbCl_2$ as minor products suggesting a reaction mechanism that incorporates $PbCl^+$ as an end product (*e.g.*, equations (5) or (6)) in the GI tract. However, the available experimental data are simulated reasonably well using the solution to equation (7) suggesting that, at least at pH 2.0, complexing of lead is of minor importance to the kinetics of PbS dissolution. The lack of experimental data where $PbSO_4$ particle size is constrained and the use of more sophisticated models that incorporate lead complexing are important topics for future research.

Conclusions and Recommendations

Mineralogical analysis and photomicrographs of soils from mining areas in conjunction with geochemical calculations indicate that lead sulfate, $PbSO_4$, will control lead solubility in mining wastes. However, lead from other anthropogenic sources may also be present in the sulfate form and may be chemically indistinguishable from mining waste lead. Photomicrographs indicate that galena crystals are often enclosed in a pyrite or silicate matrix, making them unavailable for dissolution. If this type of encapsulation is typical, then dissolution will be limited by the available $PbSO_4$ surfaces. Consequently, the use of equilibrium computer models such as MINTEQA2 will provide erroneously high dissolved lead concentrations. Furthermore, steady state dissolution may not be achieved during the relatively rapid passage through the stomach and gastro-intestinal tract. The short GI transit period implies that dissolution kinetics may control lead concentration and, therefore, bioavailability. An accurate model of lead bioavailability must incorporate kinetic considerations as well as site and host-specific factors including particle size distribution, lead phase mineralogy, age, and nutritional status of the individual.

Given the significance of exposures to lead in soil and the importance of bioavailability in estimating body burden from such exposures, we believe it is important that efforts be made to develop a short-term approach for estimating bioavailability for those situations where epidemiological data are unavailable.

In addition, an *in vitro* dissolution system should developed which mimics the gastro-intestinal tract taking i pH, organic ligands and other related factors into account. T system should be tested with lead samples from soil at si where well-conducted epidemiological investigations ha been performed with a range of soil lead/blood lead slo values. The *in vitro* system could then be calibrated to yield range of solubilities or solubilization rates that are similar to t range of slope factors. Solubility information could interpreted with respect to incremental impact of lead in soil blood lead.

Development of the *in vitro* system should provi information for input parameters for quantitative models. F example, it is expected that the *in vitro* system could descri appropriate pH/Eh conditions and concentrations of ligan The quantitative model could provide estimates of soluble le based on such inputs. To be biologically plausible, such a mo should describe potential concentrations of soluble lead pres as free ions or complexed to soluble ligands. The solubility lir or rate from this type of modeling should also be considered models designed to estimate blood lead concentrations in environmental data such as the Integrated Uptake/Biokine Model. Potential uncertainties with this approach include inability to adequately quantify host specific factors such developmental status of the gastrointestinal tract or dir uptake of microparticles of lead.

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Midvale Community Lead Study

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Abstract

The primary objective of this study was to ascertain whether children living in close proximity to mill tailings and a former lead smelter site were currently exhibiting elevated blood lead (PbB) concentrations. To address this issue, the mean PbB for community children and the relationship between PbB and the proximity of the child's residence to the site was estimated. A secondary objective was to identify and quantify accessible lead (Pb) and arsenic (As) in the environment (e.g. Pb in soil, dust, paint and water or As in soil and dust). A third objective was to test for association between specific sources of environmental Pb and PbB and to estimate the relative contribution of these proximate sources of lead to the children's PbB. The data analytic methods allowed estimation of both direct and indirect impact of environmentally accessible Pb. The average PbB level of all children screened in Midvale was 5.2 μg dL^{-1}. Three percent exceeded 15 μg dL^{-1}; 12.7% exceeded 10 μg dL^{-1}. Pb-based house paint and Pb contaminated soil were identified as principal contributors to PbB. PbB was found to increase 1.25 μg dL^{-1} per 1,000 ppm increase in lead in soil. Proximity of residence to the mill and smelter site was found to be a strong predictor of Pb in soil, and therefore indirectly related to increases in PbB.

Site History and Description

The site included a former milling and smelting operation located 12 miles south of Salt Lake City, Utah. Milling or smelting operations were in effect from 1910 to 1971. The smelter (located north of and adjacent to the mill site closed in 1958; the milling operation closed in 1971. During the milling operation, sulfide concentrates of lead, copper and zinc were extracted by froth flotation from ore. The facility operated as a custom mill, receiving ore from many sources and concentrating and extracting a variety of metals.

The tailings from the milling operations are located at the mill site in piles up to 50 feet deep, covering approximately 260 acres. Arsenic, cadmium, lead, chromium, copper and zinc have been identified in potentially hazardous concentrations during previous analyses of tailings samples. Residential and agricultural areas which surround the mill site have been potentially subject to contamination directly via the air pathway, with soil becoming contaminated due to wind-deposited tailings and stack emissions during smelting operations. A potential health hazard was thought to exist as a result of direct human contact (inhalation or ingestion) with contaminated material (tailings, soil or reintrained airborne particulates).

The City of Midvale, with a total population of about 12,000, is located adjacent to the mill site and to the east. Approximately 1,440 people live within 0.25 miles of the site, and 8,180 people live within 1.0 miles. Occupied residential and commercial areas lie immediately adjacent to the mill site on the east. The study area was bounded on the east by Interstate 15 and on the west by the now inactive mill and tailings site and smelter slag piles. The northern boundary was at Eighth Street, while the southern boundary was at Tiffany Town Drive. These boundaries were selected as study boundaries because they coincided with the current natural boundaries of the neighbourhood. The study boundaries and key reference points are shown in Figure 1.

Sampling frame

Study participants consisted of children, 6 to 72 months of age, currently residing in the study area previously described. A further restriction was that they must have resided at their current address for a least 2 months. Study enrolment was voluntary. Pregnant women and nursing mothers were also encouraged to participate if they resided in the study area.

Selection of study participants

The large number of potentially eligible study participants (>250 children drawn from >200 families) precluded the necessity of testing all children in order to obtain a precise estimate of the population mean PbB and distribution. Therefore, a random sample of approximately 50% of eligible children was recruited. Random selection from among eligible families was conducted within each of the 45–50 blocks that comprised the area. Several partial blocks had as few a 5 dwelling units. Most had about 20–40 units, while a few blocks, with large apartment complexes, had over 100 units. The number of residences selected in each block was proportional to the density of eligible families in each residence type (apartment or single family) in the block. Recruitment and blood sampling occurred over a three week period in September, 1989.

This proportional random sampling strategy produced a sample that was representative of the community with respect to location of residence, type of housing and ethnic make-up of the community. Some families had more than one child in the target age range. In that case, even though all children in the family may have been tested, only one was randomly selected for estimating the mean PbB of the target group and for modelling the environmental lead/blood lead relationship.

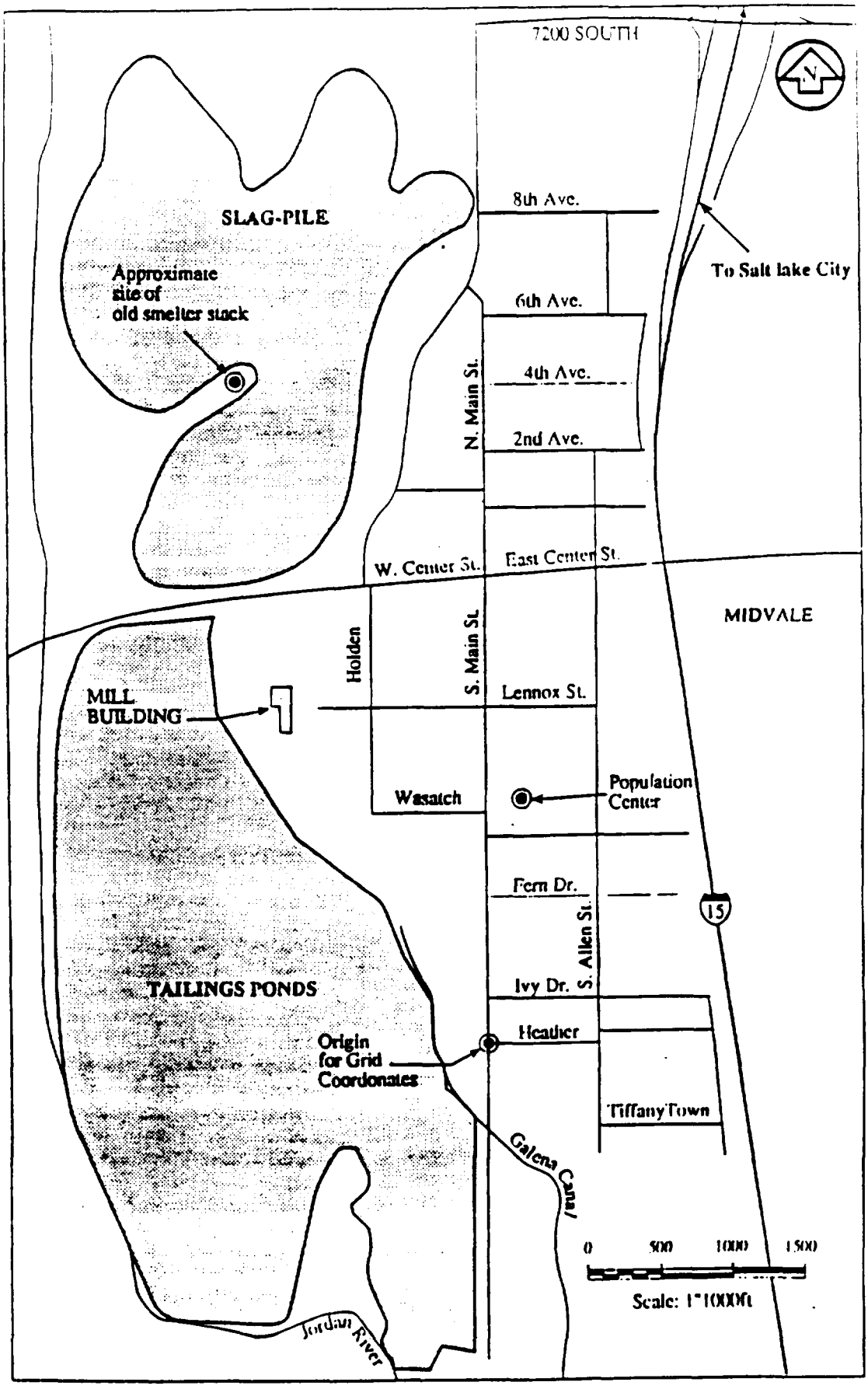


Figure 1 *Map of Midvale study area showing important reference points. See text for boundary of residential study*

Overview of Census and Interviews

Six, two-member teams were used in the collection of the census data. All census takers underwent thorough training on methods used to obtain reliable and complete data. Interpreters (Hispanic, Laotian, Cambodian and Vietnamese) were available to assist census teams. Study descriptions and announcements were prepared in several languages. An effort was made to contact all residents in the study area at their homes. In the event that no one was at home at the initial visit, the teams made two additional attempts to contact the family on different days at different times of the day.

The following represents some of the key information obtained by interview during the initial census or during a clinic interview:

(1) Current address.
(2) Names and ages of all children residing at the residence.
(3) Names and ages of pregnant women or nursing mothers.
(4) Duration of residence at current address.
(5) Type, age and condition of current housing.
(6) Parental occupation and education.
(7) Recent major renovation at current address or prior address.
(8) Frequency of childhood habits such as mouthing behaviour.
(9) Use of fill material at any site on the residential lot.
(10) Lead-related hobbies or occupations.
(11) Time spent (hours per week) at day care centers or secondary residences.

Protocol for Blood Collection, Lead Analysis and Quality Control

Whole blood samples were collected by trained pediatric phlebotomists for the analysis of lead, protoporphyrin (FEP) and hematocrit. For these analyses, 2 mL of blood was obtained using a venipuncture blood collection technique. A serum sample was obtained for possible determination of iron status in the event that the FEP was elevated.

Sample collection

Venipuncture samples were drawn using a 23 gauge butterfly apparatus attached to a 6 mL disposable syringe. Blood was immediately dispensed into a K_3 EDTA-containing pediatric vacutainer tube by insertion of the needle through the top of the tube. The tube itself was the inverted several times to mix the anti-coagulant. A red top pediatric vacutainer was filled for possible iron determinations.

Sample analysis

(1) All samples were analyzed for lead in duplicate using anodic stripping voltammetry (ASV). Analyses were conducted at the University of Cincinnati using the method of Roda *et al.* (1988).
(2) The lead concentration of one in every 20 blood samples was determined by ESA Laboratories, Inc. for inter-laboratory comparison.
(3) All benchtop quality control blood samples were set up in Midvale at the same time the participant samples were prepared.
(4) Quality control samples prepared in the Cincinnati laboratory were included in all analytical runs. These samples consisted of human blood samples with lead content determined by isotope dilution mass spectroscopy, the definitive lead method.
(5) Samples whose duplicate lead values differed by more than 3 $\mu g\ dL^{-1}$ were reanalyzed. This occurred in less than 2% of the samples.

Protocol for Residential Environmental Sample Collection and Analysis

These procedures address the sampling of water, interior and exterior lead-based paint, household interior surface dust, exterior surface dust and soil. Details of methods development and their application in other lead exposure situations can be found in Que Hee *et al.* (19895); Clark *et al.* (1985); Bornschein *et al.* (1985); Bornschein *et al.* (1989).

Lead paint (PbB) screening

Screening of interior and exterior surfaces were done with an X-ray fluorescence lead-in paint analyser (referred to as an XRF); the model XK-2 and XK-3 manufactured by Princeton-Gamma Tech were used. These instruments measure lead in paint on an area basis, as mg Pb cm^{-2}. Three readings per surface were made. At least one wall and one trim in each of the primarily occupied areas (entry room, living room, child's room) of the residence were screened. Three surfaces were evaluated on the outside. Thus nine surfaces in and around a residence were measured in triplicate. Unpainted surfaces were not screened. These included panelling, wallpapered walls, unpainted brick and unpainted sidings, wood or other non-paint finishes.

Interior household surface dust

Interior surface dust was sampled using a small vacuum pump to obtain dust from measured areas. The dust collected may have arisen from household and/or non-household sources. The amount of dust obtained was weighed and the lead content of the dust expressed as either ppm (weight content) or $\mu g\ m^{-2}$ (area content). The relative dustiness of the sample areas may be expressed as weight of dust collected per unit area.

A composite sample was obtained from three measured areas frequented by the children in the residence. The areas were:

(1) A floor directly inside the main entry to the residence.
(2) A floor in the most frequently occupied room (usually the living room or kitchen).
(3) A floor area in the child's bedroom.

Field duplicates were obtained at 10% of the residences.

Exterior surface dust and soil

Two types of samples were obtained, representing different surface conditions. Soil cores of 2 cm depth were taken in grassy areas, gardens and play areas, while composite surface dust samples were taken with a vacuum apparatus on paved areas and other hard surfaces near building entries, *e.g.* front and rear entrances.

A composite sample of soil cores was taken from grassy yards adjacent to a residence, *i.e.* from each of front, back and sides, for a maximum of 12 samples per composite. Cores were taken at equal spacings along the sides of the building, at a distance of three feet from the building wall. Soil reflecting paint contamination is found in close proximity to the building.

Small lot sizes and fences precluded taking building perimeter samples greater than 3 feet on many properties. For large apartment buildings, proportionally more composited samples were taken. A composite sample of soil cores was also collected from cultivated areas accessible to children, obvious play areas or sand boxes, and from bare soil areas in the yard. Field duplicates were collected at 10% of the sample sites. For the purpose of model construction, the maximum soil lead sample (PbS_{MAX}), irrespective of location on the residential lot, was also tested for its association with PbB.

Soil samples were air dried over night. They were then sieved into fractions: a "Total Soil Fraction" which passed a 2 mm sieve and a "Fine Fraction" which passed a 250 µm sieve. Samples were dried to a constant weight prior to obtaining aliquots for analysis. Samples were digested in 50 mL of 7N HNO_3 for 2 h, taken up in 100 mL of 1N HNO_3 and analysed by atomic absorption spectrometry.

Water sampling

Two Fixed First Draw (30 minute stagnation) water samples were collected from the primary water faucet, normally the kitchen sink. These samples were collected 30 minutes *after* the water was first allowed to run for about three minutes. A 250 mL sample was taken immediately upon opening the tap without wasting any water. A second 750 mL sample was taken immediately after the first sample , without wasting any water between sample No.1 and sample No.2. Field duplicates were collected at 10% of the residences.

Spatial location of residence using Assessor's Office plat maps

Each single family residence or apartment building is identified by a unique number in the Property Assessor's Office. The number consists of a Section number, Block number and Individual Property number. This information was used to link all residential environmental blood lead data. In addition, the information permitted us to locate each residence on aerial photograph-plat maps available through the Assessor's Office. The photo maps, at a scale of 1 inch = 100 feet, permitted us to locate each residence relative to the site. It was then possible to directly measure the distance from several suspected lead sources, *e.g.* the distance from the former smelter site (DS) or from the mill building (DM) to each residence. The accuracy of the measurements was within ±25 feet, or about 2% error at 2,200 feet, the average distance from a residence to the mill building.

Spatial location by use of a grid coordinate system

The procedure of measuring distances from residence to specific loci such as the mill building has the disadvantage that an infinite number of such loci can be identified. More importantly, it presumes that the contaminants originated from a single point source and dispersed in a radial pattern from the point source. Because of these problems it was decided that each residence should be assigned a North/South–East/West coordinate as measured from the aerial plat map. The coordinate system has as its origin the intersection of South Main Street and Heather Street. Distances were measured in feet in positive increments proceeding North or East and in negative increments proceeding South or West. Use of such a coordinate system permitted a direct test of the hypothesis that soil lead or blood lead concentrations were randomly distributed. Conversely, a gradient in such concentrations could be quantified on both East/West and North/South dimension.

Data Analysis

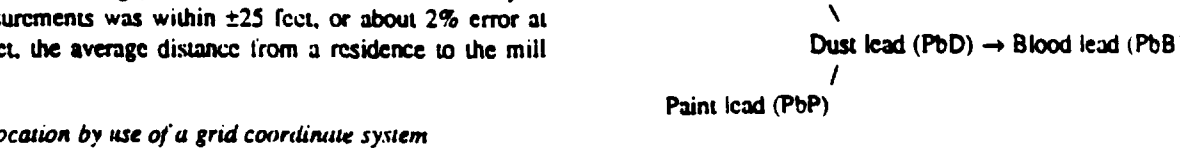
Descriptive statistics

The frequency distribution of PbB and the environmental data were plotted for visual inspection. PbB and environmental Pb and As data were transformed to their natural logarithm and estimates of the sample geometric mean and geometric standard deviation were calculated. The PbB distribution, statistically adjusted for the age of the sampled children was also obtained. These distributions were compared to available norms (Mahaffey *et al.*, 1982; CDC, 1985). Simple bivariate correlations among the exposure variables, covariates, confounders and dependent variables were calculated.

Inferential techniques

Since one of the purposes for collecting these data was to identify proximate sources of lead responsible for elevated body burden (as measured by PbB), methods for assessing PbB and environmental Pb were used. However, even where environmental Pb sources and PbB are statistically correlated, a causal, readily interpretable model necessarily results when all major sources of possible Pb contamination are surveyed and entered into a statistical model, neither the contribution of individual sources to PbB nor the means by which these sources might be affecting children's PbB levels can be determined.

One method for statistically demonstrating pathways of Pb exposure and transport is the technique of structural equation modelling. This methodology allows the postulation of both final outcomes (PbB in this case) and intermediate variables (*e.g.* dust lead) which serve as mediators of lead exposure. These intermediate variables may be both predictors of the final outcome and also be consequences of other predictors. For example, in the Cincinnati urban cohort study, the following model was found to explain the environmental Pb and PbB data collected from a group of 18-month old children (Bornschein *et al.*, 1986).



$$Ln(PbB) = a_1 + b_1 ln(PbD)$$

where: $Ln(PbD) = a_2 + b_2 ln(PbP + b_3 ln(PbS)$

This model suggests that dust serves as an intermediate repository for lead that emanated originally from exterior soil and paint, since no direct path from soil or paint was found. The methodology allows testing for the direct contributions of a lead source to body burden, as well as the indirect contribution of a source to the intermediate but environmentally available pool of lead in and around the residences of young children.

The Midvale study data are correlational in nature, meaning that additional covariates, such as child's age and duration of residency, needed to be taken into account. See Table 1 for a list of key variables examined. In addition,

Table 1 *Variables examined in developing the blood lead model.*

Name	Description	Units
Exposure variables		
PbB	Venous blood lead	$\mu g\ dL^{-1}$
PbD_{INT}	Residential interior house dust	ppm or $\mu g\ cm^{-2}$
PbD_{EXT}	Residential exterior entry dust	ppm or $\mu g\ cm^{-2}$
PbS_{MAX}	Maximum soil lead at residence	ppm
PbS_P	House or apt. perimeter soil lead	ppm
PbS_G	Garden soil lead	ppm
PbS_B	Bare area soil lead	ppm
PbS_S	Play area soil lead	ppm
PbW	Tap water lead	ppb
XRF_{INT}	Interior paint lead by XRF	$mg\ cm^{-2}$
XRF_{EXT}	Exterior paint lead by XRF	$mg\ cm^{-2}$
Biological, social demographic and behavioral covariates:		
TIBC	Total iron binding capacity	$\mu g\ dL^{-1}$
Hct	Hematocrit	percent
WIC	Participation in food suppl. prog.	y/n
HA	House age	years
SES	Socioeconomic status	
RT	Duration of residence at same address	months
Age	Child's age	months
Gender	Child's sex	1=male; 2=female
Ethnicity	Maternal race	
DM	Distance from mill to residence	feet
DS	Distance from smelter to residence	feet
LOC	Location of residence relative to reference point	(NS, NS^2, EW, EW^2)
Eating vegetable crops		y/n
Hours away from home		y/n
Use of soil fill		y/n
Air conditioning		y/n
Use of folk medicines		y/n
Mouthing behaviors		y/n
Paint removal		y/n

Footnotes:
Interactions of age, age², RT, RT², mouthing behaviors, hours spent away from home and vegetable consumption with exposure variables were also examined.
y/n = yes or no.

interactions of age, the quadratic term, age^2, residence time (RT) and $(RT)^2$, hours spent away from the primary residence and behavioural variables (*e.g.* mouthing) with the exposure variables (PbD, PbS, PbW, XRF, location) were also examined in the regression model. This provided for possibly non-equivalent effects of the environmental variables across the age, residence time or behavioural spectrums, while allowing all of the available data to be evaluated simultaneously. From this initial regression model, insignificant ($p > 0.5$) interaction terms or main effects not comprising any interaction variable were pooled with error. At the final step, a single structural model involving PbB and all environmental Pb variables found to effect PbB as exogenous variables was fit. Only significant main effects and interactions or the main effects involved in interactions remained in the model. All variables previously dropped from the PbB and environmental Pb equations were considered for inclusion at this step, by regressing each of the residuals from the structural equations on these excluded variables. Such an approach maximises the power to discern any contribution of these environmental sources of Pb to body burden, while estimating a model which reflects our current understanding of Pb migration and exposure, and allowing other behavioural or demographic factors to be considered. This strategy has been followed in our previous publications (Bornschein *et al.*, 1985; Dietrich *et al.*, 1986; Bornschein *et al.*, 1986; Bornschein *et al.*, 1989).

Consent

This study was reviewed and approved by the University of Cincinnati Medical Center Human Research Committee. All participants were presented with a brief description of the protocol and asked to sign a consent form.

Results

Blood lead results

Ninety-seven percent of the families contacted during the Midvale census agreed to be interviewed. The door-to-door census revealed 249 children (less then 72 months of age) living in the study area, as well as 43 pregnant women and 22 nursing mothers. During the course of the subsequent blood lead screening program, 73% of the children, 42% of the pregnant women and 77% of the nursing mothers living in the study area had their blood tested for possible elevations in lead (see Table 2). A total of 292 individuals of all ages were screened. Table 3 summarizes the blood lead levels found during the course of testing. The average (geometric mean: GM) blood lead level of *all* children (a non-random sample) less than 72 months of age was found to be 5.2 $\mu g\ dL^{-1}$. The geometric standard deviation (GSD) was 1.66 with a range of observed blood lead levels from 0.5 to 22.5 $\mu g\ dL^{-1}$. This value is very similar to the estimate of average blood lead levels of 4.0–6.0 $\mu g\ dL^{-1}$ in children in the United States without unusual sources of exposure in 1990 (US EPA, 1989). Pregnant women and nursing mothers also had very low blood lead levels with none exceeding 4.5 $\mu g\ dL^{-1}$. The current level of concern for these sensitive populations is 10–15 $\mu g\ dL^{-1}$ (ATSDR, 1988).

The random selection process resulted in a random sample of about 60% of the families in the study area with one or more children less than 72 months of age. In some cases, families had more than one eligible child in that category. Since blood lead levels within families are correlated ($r = 70$; see Montana Dept Health, 1986), it was necessary that only one child per family be randomly selected and used in estimating the community blood lead level for children. This process yielded a random sample of 128 children, one child per family. In a few cases, families moved prior to the completion of the environmental survey. In others, the family did not grant permission for the sampling team to enter the residence, and in one case an apartment building owner did not grant permission to the sampling team to collect exterior dust and soil samples. These events resulted in some missing interior or exterior environmental data. While it might be possible to substitute community average values for these missing data points, the

Table 2 *Recruitment summary*

Number of families randomly selected to participate	134
Number of families refusing to participate	14
Number of randomly selected replacement families	9
Number of additional families requesting lead screening ("volunteers")	7
Total number of families screened (random sample + volunteers)	136
Total number of children screened (>6 and <72 months)	181
Number of pregnant women screened	18
Number of nursing mothers screened	16
Number of other adults	43
Number of older children screened (>72 months)	33
Total number of individuals screened	291
Total number of children <72 months	181
Children in volunteer families	−15
Siblings randomly excluded	−38
Families excluded because of incomplete environmental data	−16
Data set with randomly selected participants and complete data	112

more statistically conservative approach was taken, *i.e.* any case with missing data was dropped from subsequent analyses. This resulted in a final set of 112 children with complete blood lead, interview, exterior and interior environmental data. Figure 2 illustrates the blood lead distribution of the study (n = 128; GM PbB = 4.9 μg dl^{-1}).

Environmental results

Table 4 summarizes the results of analyses of interior and exterior samples for lead and arsenic for the 112 households in the random sample. Not all of the residential yards (or gardens, bare areas or play areas, thus the number of observations (n) for these sample types are less than 112: 46, 88 and 42 respectively. With the exception of the randomly dispersed samples, environmental lead concentrations were found to be well below those reported for older mining communities or active smelter sites. Of all the dust and soil samples, 13% contained >1,000 ppm Pb and less than 2% contained >2,000 ppm Pb. In one older home built prior to 1911, attic dust was sampled and found to contain over 10,000 ppm Pb. Young children resided in this house. The dust probably originated from smelter emissions at the turn of the century. Older residences in the community may have similar accumulations in attics and eaves. While elevated levels of lead in paint (>1.0 mg Pb cm^{-2} of surface area) were found, they tended to be confined to older houses, most of which were located along Center Street. For those residences where no paint was found, *e.g.* aluminium mobile homes, the lead in paint was reported as 0.0 mg Pb cm^{-2}.

Thirty-six percent of the residences were found to have interior or exterior paint lead concentrations >1.0 mg cm^{-2}, indicative of the presence of lead-based paint. Soil lead

Table 3 *Blood lead distribution by group and age of child.*

Distribution by group

Group	n	GM	GSD	Minimum	Maximum
6–72 month old	181	5.2	1.66	0.5	22.5
6–18 month old	33	3.9	1.62	0.5	14.5
Adults	43	2.2	1.77	0.0	8.0
Pregnant women	18	1.6	1.43	0.5	3.5
Nursing women	16	2.3	1.67	0.0	4.5

Distribution by age of child

Age range (months)	Midvale Random sample[1] Average[4]	Midvale Random sample[1] Maximum	Midvale Total sample[2] Average[4]	Midvale Total sample[2] Maximum	Telluride Total sample[3] Average[4]	Telluride Total sample[3] Maximum
<12.0	3.7	13.5	3.4	16.5	5.4	16.0
12.1–24.0	5.5	16.0	5.2	22.5	7.1	18.0
24.1–36.0	5.0	14.0	6.0	19.5	6.4	10.5
36.1–48.0	5.2	16.0	4.9	16.5	6.6	19.0
48.1–60.0	5.4	13.0	5.2	18.0	5.6	11.5
60.1–72.0	4.1	8.5	4.9	13.5	5.5	13.0

[1] n = 112 (random sample with complete environmental data).
[2] n = 181 (random sample + siblings + volunteers)
[3] n = 94 (Bornschein *et al.*, 1989) – shown for comparison.
[4] geometric mean.

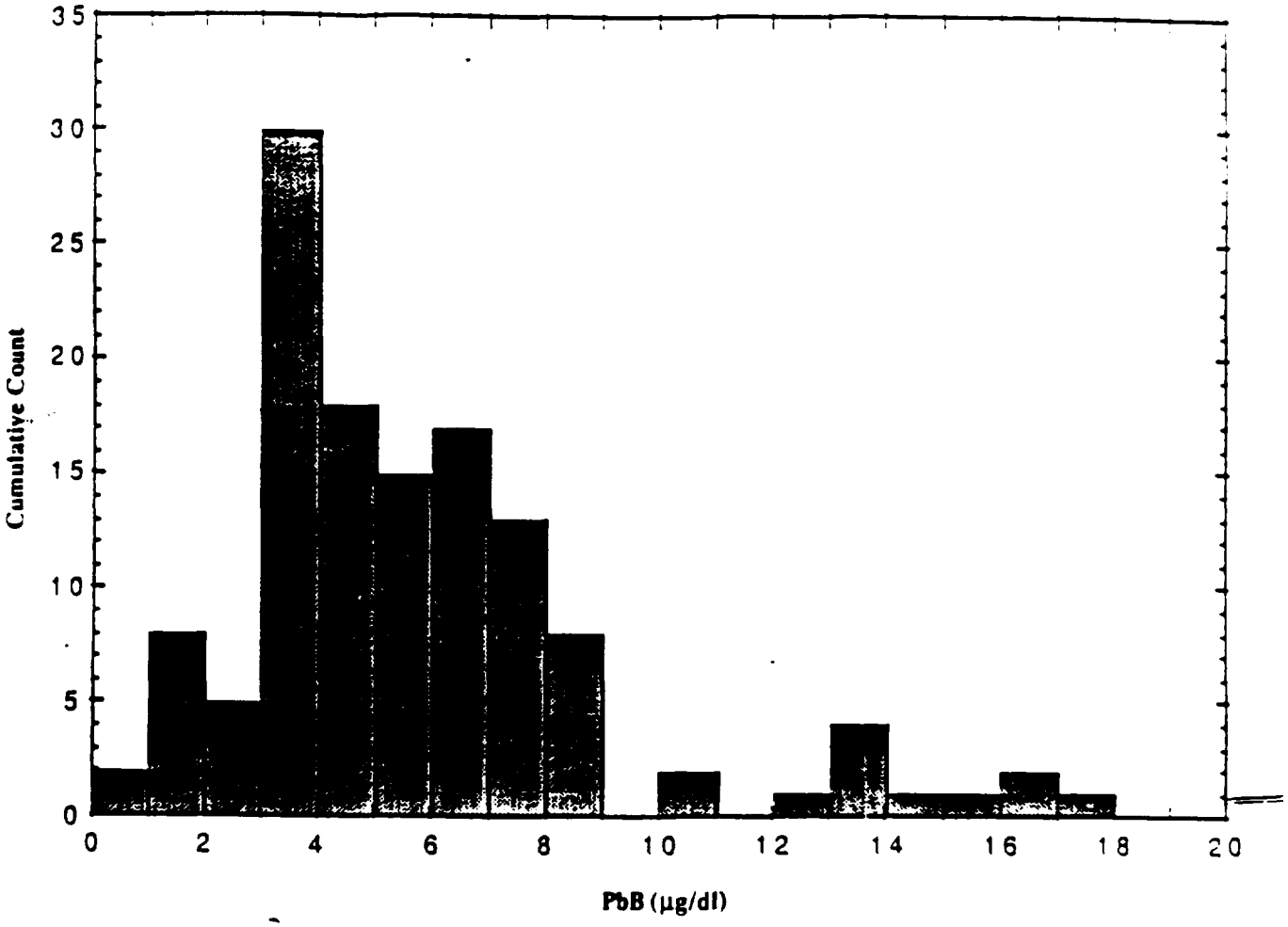


Figure 2 *Histogram of blood lead concentrations for the 128 randomly selected study participants (one child per family).*

Table 4 *Descriptive statistics for environmental lead and arsenic concentrations in residential samples.*

	n	GM	GSD	Minimum	Maximum
PbS$_{MAX}$	112	398.91	2.54	58	6,665
PbS$_{P}$	112	341.81	2.45	58	1,989
PbS$_{G}$	46	294.59	2.65	57	2,746
PbS$_{B}$	88	313.20	2.60	24	2,920
PbS$_{S}$	42	77.95	5.52	1	6,665
PbD$_{INT}$	112	437.70	1.91	119	3,602
PbD$_{EXT}$	112	466.16	2.39	79	2,984
PbW	112	1.43	1.92	1	48.5
XRF$_{INT}$	112	1.00	1.75	0	20.4
XRF$_{EXT}$	112	1.24	1.63	0	14.9
AsS$_{P}$	112	35.78	1.98	8	211
AsS$_{G}$	46	34.25	2.28	10	291
AsS$_{B}$	88	34.34	2.32	8	356
AsS$_{S}$	42	12.39	2.75	3	118
AsD$_{INT}$	112	22.36	1.95	5	157
AsD$_{EXT}$	112	39.42	2.20	2	318

Table 5 *Average blood lead and soil lead by geographic quadrant.*[1]

	Northwest	Northeast
n	42	23
SES	24	27
Age (months)	31	36
PbS (ppm)	612	441
PbB ($\mu g\ dL^{-1}$)	5.77	5.78
PbB (>10 $\mu g\ dL^{-1}$)[2]	4 (10%)	2 (9%)
PbB (>10 $\mu g\ dL^{-1}$)[3]	11	2
	Southwest	**Southeast**
n	24	39
SES	23	30
Age (months)	34	35
PbS (ppm)	592	130
PbB ($\mu g\ dL^{-1}$)	5.27	3.80
PbB (>10 $\mu g\ dL^{-1}$)[2]	5 (21%)	1 (3%)
PbB (>10 $\mu g\ dL^{-1}$)[3]	7	3

[1] Origin (center) of the four quadrants is at 1700 N, 335 W, approximately the center of the block bounded by South Main, East Lennox, S Allen and Wasatch Avenue. The origin is the population center for the random sample of children.
[2] Number of children from *random* sample with PbB > 10 $\mu g\ dL^{-1}$ (n = 128).
[3] Number of children from *total* sample with PbB > 10 $\mu g\ dL^{-1}$ (n = 181).

Table 6 *Correlation coefficients*[*] *for ma[illegible]*

	PbS_{max}		PbB	
	r	p	r	p
PbS_{MAX}	–	–	0.32	0.000[illegible]
PbS_P	0.96	0.0001	0.30	0.001
PbS_G	0.05	0.60	–0.01	0.95
PbS_S	0.16	0.10	0.22	0.02
PbS_B	0.39	0.0001	0.14	0.13
PbD_{EXT}	0.77	0.0001	0.16	0.09
PbD_{INT}	0.74	0.0001	0.19	0.05
XRF_{EXT}	0.43	0.0001	0.19	0.04
XRF_{INT}	0.36	0.0001	0.15	0.12
SES	0.16	0.09	–0.39	0.0001
N–S	0.68	0.0001	0.25	0.007
E–W	–0.74	0.0001	–0.24	0.01
DM	–0.68	0.0001	–0.20	0.03
DS	–0.60	0.0001	–0.23	0.02
DMPL	–0.07	0.49	–0.04	0.69
DMSPL	–0.45	0.0001	–0.08	0.41

DM = distance to mill building (+2150 N; –1350 W
DS = distance to smelter stack (+4400 N; –1750 W
DMPL = distance to mill property line.
DMSPL = distance to mill or smelter site property li[illegible] whichever was closer.
N–S = grid coordinates; units (feet) increase in [illegible] direction from S to N.
E–W = grid coordinates; units (feet) increase in [illegible] direction from W to E.
[*] all lead variables were log transformed.

>6.0 mg Pb cm^{-2}, indicating very high levels of lead in paint.

Arsenic concentrations were higher than reported for urban studies and reflect the milling and smelting activities which prevailed for many years in and around Midvale. Lead and arsenic concentrations were generally highly correlated (r = 0.82–0.93) within each sample type. This strongly suggests that the elements have been travelling together, perhaps in the same particles. In the case of interior floor dust samples, the correlation between PbD and AsD was weakest (r = 0.82), possibly reflecting an additional lead source, *e.g.* lead-based paint, contributing to lead dust in some but not all residences.

Table 5 summarizes the soil lead and blood lead concentrations and frequency of elevated levels in the four geographic quadrants surrounding the calculated center of the sample. The population center of the random sample of children examined in Midvale was located at coordinates +1700 N and +335 W, a point approximately in the center of the block bounded by South Main, East Lennox, South Allen and Wasatch Avenue.

Table 6 summarizes the correlation between environmental and/or social variables of main interest and the maximum soil lead concentration found at the residence, and the child's blood lead. Environmental soil and dust lead concentrations were generally moderately correlated (r = 0.5–0.8). Correlations between environmental lead and blood lead concentrations were considerably weaker (r <0.35).

The strongest correlates of blood lead we economic status (SES) and PbS_{MAX}. Location of the based on grid coordinates was also related to blood l distance from the mill building (DM) and site of smelter stack (DS) were only weakly associated with distance from the mill property line (DMPL) was a PbB. It should be noted that these correlations are [illegible] for any other factors.

Environmental lead/blood lead relationship

In order to adjust for known or suspected collinear variables in this data set, ordinary least square regression analyses were performed. The analyses i an extensive set of potential predictor variables, inclu interactions (see Table 1). Non-significant varia removed from the prediction equation by the p backward elimination, one variable at a time. completion of this process and the formulation reduced regression model, each previously elimina was re-tested for possible re-entry into the reduced m process was used to derive prediction equations or models for each of the environmental soil and dus both lead and arsenic. This resulted in 12 separate equations. The final models were quite similar for e type. The results indicate that location of residence and amount of lead-based paint are common predic

Table 7 *Regression parameter estimates of lead in perimeter residential yard soil (PbSp) and interior house dust (PbD) (n = 112).*

Independent	Estimate	Standard error	t	p	R^2
Dependent: ln(PbDi)					
Intercept	2.873	0.284	–	–	–
ln(PbSp)	0.568	0.049	11.65	0.0001*	0.501
ln(XRFEXT)	–0.222	0.115	–1.93	0.06	0.014
Rmve paint	–0.131	0.128	–1.03	0.31	0.004
ln(XRFEXT) times rmve paint	0.331	0.143	2.31	0.01*	0.020
				Unresolved shared variance	0.066
				Total variance accounted for (R^2)	0.605
Dependent: ln(PbSp)					
Intercept	6.261	1.33	–	–	–
ln(XRFEXT)	0.179	0.078	2.31	0.01*	0.008
East/West	–0.0009	0.00006	–15.73	0.0001	0.358
North/South	0.0001	0.00002	4.22	0.0001	0.026
Housing age**		F(2,106) = 17.16		0.0001	0.050
19th century	0.040	0.157			
Post-WWII	–0.567	0.101			
				Unresolved shared variance	0.405
				Total variance accounted for (R^2)	0.847

* One-tail p-value.
Coded as follows: 19th century yes = 1; no = 0,
Pre-WWII yes = 1; no = 0,
Post-/WWII yes = 1; no = 0.
** Intercept assumes Pre-WWII housing.

in environmental samples. The explanatory power of these statistical models were generally quite high, *i.e.* the variance in lead concentration accounted for by the independent predictor variables ranged from 60 to 90%. The regression equations for lead in dust and soil are given in Table 7.

In developing a final regression model for describing the relationship between environmental factors and PbB, we took note of the fact that location of residence was a strong correlate of maximum soil lead concentrations (PbS_{MAX}) found on the residential property, and PbS_{MAX} was the strongest environmental correlate of PbB. We therefore tested the possibility that location of residence indirectly affected PbB through its influence on soil lead concentrations or dust lead concentrations. The statistical method for testing for the presence of both direct and indirect pathways such as this is called structural equations or systems equations analysis. This data analytic technique involves the simultaneous estimation of two or more related regression equations. Once again, the full list of variables and interactions listed in Table 1 were evaluated. The qualitative results of this analysis are shown in Figure 3.

The analysis supported the hypothesis that location of residence indirectly impacted PbB through its relation to PbS_{MAX}, even though there was no discernible direct impact of location of residence on PbB. In Figure 3, the presence of an arrow between two variables indicates the presence of a covariate-adjusted statistically significant association between the two variables. Conversely, if there is no linking arrow, there is no direct association between the variables. For example, there is no direct association between location of residence and PbB. However, they do indirectly influence PbB. Table 8 contains the two system equations used to predict

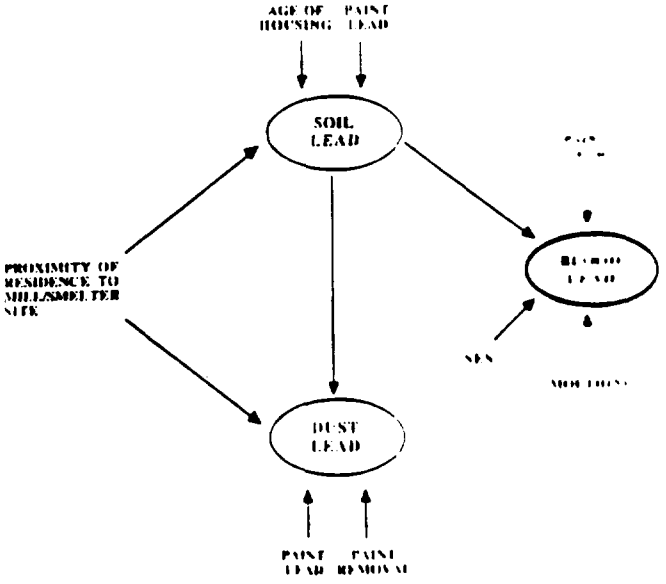


Figure 3 *Path diagram illustrating variables influencing soil lead, dust lead and blood lead. Arrows indicate statistically significant associations.*

Table 8 Two-system equations used to explain PbB (n = 172)

Exogenous	Estimate	Standard error	t	p	R^2
Dependent: ln(PbB)					
Intercept	1.159	0.363	–	–	–
ln(XRF$_{EXT}$)	0.164	0.095	1.73	0.04*	0.019
ln(PbS$_{MAX}$)	0.114	0.057	1.99	0.02*	0.030
SES	–0.016	0.004	–3.80	0.0001*	0.097
Mouths cigarettes	0.090	0.034	2.62	0.005*	0.045
			Unresolved shared variance 0.087		
			Total variance accounted for (R^2) 0.278		
Dependent: ln(PbS$_{MAX}$)					
Intercept	6.329	0.139	–	–	–
ln(XRF$_{EXT}$)	0.301	0.081	3.73	0.0002*	0.020
East/West	–0.0009	0.00006	–14.91	0.0001	0.321
North/South	0.0001	0.00003	4.51	0.0001	0.029
Housing age		F(2,106) = 16.10		0.0001	0.046
19th century	–0.096	0.164			
Post-WWII	–0.588	0.105			
			Unresolved shared variance 0.431		
			Total variance accounted for (R^2) 0.847		

* One-tail p-value

PbS$_{MAX}$ and PbB. There are four factors which predict PbB: (1) level of lead in exterior house paint; (2) maximum level of lead in residential soil; (3) the families' socio-economic status; and (4) a behavioural factor – "child mouths cigarette butts". The last variable "child mouths cigarette butts" may be spurious. Although statistically significant (p <0.02), it was the only mouthing variable, of 11 examined, that attained significance. Furthermore, this positive relationship with blood lead was no longer significant when the sample was expanded to include siblings (p = 0.16).

The total variability in PbB explained by all significant factors amounts to 27.8%. PbS$_{MAX}$ accounts for a minimum of 3% of the variance and a possible maximum of 10.2%. The effect of location on PbS$_{MAX}$ and PbB can be seen by first substituting average house age and maximum exterior paint lead into the regression equation for PbS$_{MAX}$. Then by substituting various East/West and North/South coordinates into the equation, one can generate expected soil lead concentrations at various residential locations throughout the area. Similarly, various PbS$_{MAX}$ values can be substituted into the PbB equation and resultant expected PbB values can be estimated for the average child (obtained by substituting average SES, XRF$_{EXT}$ and mouthing scores into the equation) or a 'high risk' child (obtained by substituting a low SES, high XRF$_{EXT}$ and high mouthing scores into the equation.

The preceding procedure was used to generate the expected values for PbS$_{MAX}$ and PbB shown in Table 9. Expected PbS$_{MAX}$ values fall quickly (and in a non-linear fashion) as one moves from a site close to the mill building (1,200 feet W, 2,400 feet N) to a site furthest East (1,200 feet E, 2,400 feet N). A similar, albeit smaller, decline is seen as one moves from the northern-most site in the study area to the southern-most site. Highest expected soil lead values are obtained in the area immediately adjac[illegible] between Lennox Avenue and Cen[illegible] 1,800–2,000 ppm Pb). Lowest expected [illegible] obtained in the south-east quadrant of th[illegible] 150 ppm Pb). Expected blood lead values [illegible] 'high risk' child follow a similar pattern. F[illegible] living nearest the site, the expected PbB [illegible] μg dL^{-1} *versus* 4.4 μg dL^{-1} in the south-[illegible] decline is statistically significant, but repres[illegible] small absolute difference in expected blood lead [illegible] From Table 9 it can be seen that for a high [illegible] difference is 3.5 μg dL^{-1}.

This small and statistically weak associ[illegible] in Figure 4. This figure illustrates the expected [illegible] lead concentrations with increasing maximum [illegible] concentration found at each residence after adjustm[illegible] factors listed in Table 8. The three lines illustrate the covariate-adjusted soil lead/blood lead relation[illegible] average child (50 percentile), the 95 percentile [illegible] percentile, based on the observed geometric standard of 1.66 μg dL^{-1}. The individual data points d[illegible] *unadjusted* soil lead/blood lead relationships, *i.e.* the [illegible] values have not been adjusted for other known sources which are contributing to the children's PbB levels [illegible] and paint lead). As would be expected, about [illegible] unadjusted cases exceed the 95 percentile. As will be later, there is a considerable degree of scatter of [illegible] values around the average or 50 percentile line, consi[illegible] the *weak association* shown in Table 8 with only 2[illegible] variance in blood lead being solely attributable to soil weak association is in part due to our inability to ide[illegible] certainty that soil and dust to which the child [illegible] exposed. The apparent lack of a direct dust lead to [illegible]

Table 9 *Expected blood lead level for the high risk child[*] estimated from the system equation for PbS_{MAX} at various grid locations in Midvale.*

North/South (feet)	1,200 West	600 West	(feet) Main St	600 East	1,200 East
5,400 N	**	**	12.55	11.81	**
4,800 N	**	**	12.44	11.70	**
4,200 N	**	13.11	12.33	11.60	**
3,600 N	**	12.99	12.22	11.50	**
3,000 N	13.69	12.88	12.11	11.39	**
		Center Street			
2,400 N	13.57	12.76	12.00	11.29	10.62
1,800 N	**	12.64	11.90	11.19	10.53
1,200 N	**	12.54	11.79	11.09[a]	10.44[a]
600 N	**	**	11.69	11.00[a]	10.34[a]
Heather Lane	**	**	11.58	10.90[a]	10.25[a]
600 S	**	**	11.48	10.80[a]	10.16[a]

[*] Assumes low SES (SES = 11), high paint lead (6 mg cm^{-2}), 19th century housing, child mouthing inedible material more than once per week.

[**] falls outside the study area, *i.e.* no housing units at this location.

[a] Note that this area contains no 19th century housing. Therefore this value is an over-estimate of expected blood lead for children in this area.

pathway might also reflect sampling error since such a path was hypothesized and has been found in other studies. The effect size (the estimated increase in blood lead for any given increase in soil lead concentrations) is also quite small. Over the range of soil concentrations from 156 ppm to 1,022 ppm (the mean $PbS_{MAX} \pm 1$ GSD) the average blood lead increases at a rate of 1.1 μg dL^{-1} per 1,000 ppm increase in soil lead.

The final model was also fit to the entire data set, *i.e.* the data set containing not only the randomly selected subjects, but also their previously excluded siblings. This was done due to concerns that exclusion of siblings with elevated blood lead levels might result in an underestimate of the soil lead/blood lead relationship. When the additional 38 siblings were included in a weighted analysis, the model explained *less* of the observed variance in blood lead, 16.3% *versus* 27.8%. The expected blood lead levels at the 95 percentile were also lower than in the original and more statistically correct analysis, *e.g.* 12.11 *versus* 13.33 μg dL^{-1} at 2,000 ppm lead in soil. Thus, the addition of siblings to the data set resulted in a model which explained less of the observed variability in blood lead levels among the children and slightly reduced the estimated blood lead levels associated with high soil lead concentrations.

The final model was also fit using distance to the smelter and distance to the mill as estimates of residential soil lead concentrations in place of the grid coordinates used in the analysis shown in Table 8. This alternative model accounted for only slightly less variance than the original model but required more terms, *i.e.* the new model was less parsimonious. This suggests that the migration or dispersion of lead from the two sites is not fully explained by the simple radial dispersion implied by this model.

Discussion

Anytime a random sample of children are surveyed for lead exposure, a relatively wide range of blood lead levels will be detected. There are several reasons why children living in the same community have different levels of lead in their blood. First, they may be *currently* exposed to different amounts of lead from their *immediate* residential environment, *i.e.* lead in soil, dust, paint, water, food or air. Second, they may be exposed to different amounts of lead encountered at secondary residences, day-care centers or schools. Children also have different behavioural patterns which influence the amount of lead intake, *e.g.* exploratory mouthing of objects, thumb sucking, fingernail biting, *etc.* Cultural differences in diet and hygiene practices can alter the amount of lead intake. Often unrecognised is the fact that fetal lead exposure or lead exposures incurred at previous residences contribute to total lead burden. These past exposures are reflected to varying degrees in current blood samples. Finally, analytical error in the measurement of lead in blood can add to the observed variability in community blood lead levels.

It is sometimes mistakenly assumed that blood lead only indicates very recent exposure. "However, blood lead levels also give information on the relative level of exposure at more remote time periods" (ATSDR, 1988). Repeat blood sampling over time, such as takes place in the prospective childhood lead studies (Bornschein *et al.*, 1985) has revealed a high degree of inter-correlation among repeat sampling. In fact, blood lead levels in 6.5 year-olds are correlated ($r = 0.72$) with lead exposures occurring five years earlier (Schroeder and Hawk, 1985; Mushak, 1989). Blood lead measurements even reflect to some extent the level of lead exposure incurred during the fetal period (Bornschein and Krafft, 1985). Thus, the geometric mean blood lead obtained in a large random sample, such as that obtained in Midvale, is a reflection of past and current exposures of the average child in the community.

Since a random sample of children was measured, the geometric mean blood lead and the geometric standard

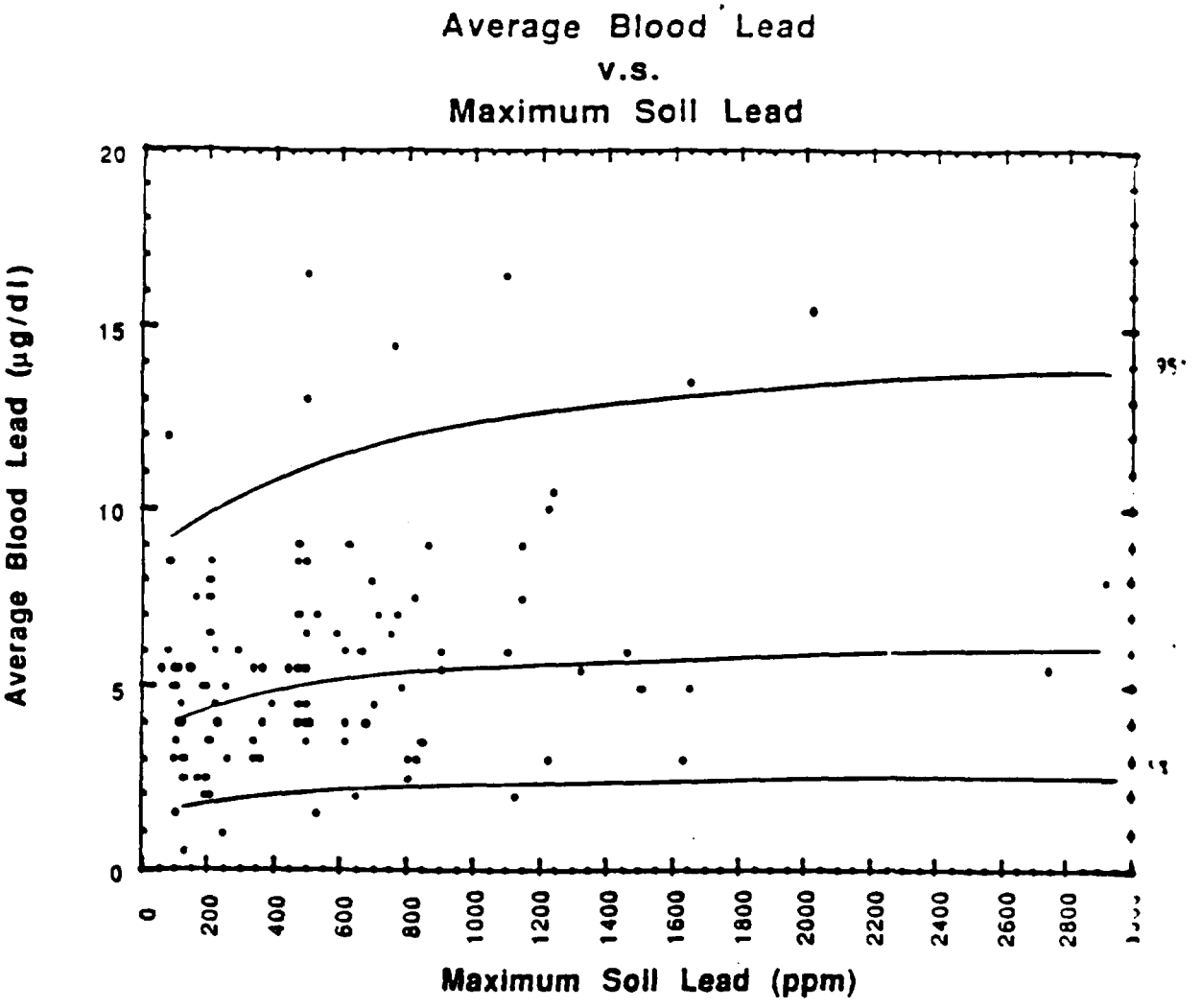


Figure 4 *Covariate adjusted relationship between soil lead (PbS_{MAX}) and blood lead as determined from [illegible] Table 8. The individual data points are not adjusted for covariates.*

deviation can be extended to represent all of the children in the Midvale study area. Taken in conjunction with the extensive characterisation of lead sources and factors which modify exposures, this study provides a detailed view of lead exposure in both low and high risk children as a result of both present and past exposures. Because of the documented breadth of exposures and highly varied mix of risk factors observed in this randomly selected cohort, it is unlikely that future patterns of exposure or levels of exposure are going to deviate significantly from that which has been observes in the present study. More importantly, it is unlikely that future generations are going to encounter greater exposures or exhibit more risk factors than has already been detected within the present community. The most likely trend in future community blood lead levels will be a decline of about 5–10% per year. This decline is an ongoing reflection of the reduction in the amount of lead being introduced into the environment as a result of regulatory actions to reduce lead in gasoline, air emissions, food and drinking water. This decline has been going on for over a decade, and has been seen in communities around the world, irrespective of the level of lead exposure or sources in the community (Bornschein *et al.*, 1989; EPA, 1986).

Current estimates are that 1990 national average blood lead levels in children not subjected to unusual [illegible] *e.g.* lead-based paints or high lead in drinking [illegible] 4.0–6.0 µg dL^{-1} (EPA, 1989). The average blood [illegible] found in Midvale was 4.9 µg dL^{-1}. This level [illegible] children exposed to an average level of 400 ppm [illegible] residential soil. The expected blood lead level of the child exposed to 60 ppm lead in soil (the lowest level can be estimated from the Midvale regression [illegible] (Table 8) to be 4.0 µg dL^{-1}, *i.e.* at or below current [illegible] of the background blood lead level.

The low blood lead levels found in the Midvale may be in part a reflection of the low physical availability the lead contaminated soil. That lead which is found particles (>250 mm) is less subject to inadvertent [illegible] Even if ingested, large particles release less of their lead per unit time than smaller particles. Even when the contained in smaller particles, it may not readily bioavailable the lead is in the form of lead sulfide embedded in matrix (galena or tailings), since stomach acid does not dissolve the surrounding quartz. Finally, there may protective effects produced by the high levels (90–2,900 ppm) which are also found in this soil. Studies shown that high dietary zinc intake reduces lead a

(Cerklewski and Forbes, 1976). Previous studies of metals in Midvale soils have shown that levels of zinc in the soil range from 90–2,900 ppm, a range and distribution pattern which parallels that of lead in soil. This zinc probably came from the same milling and smelting operations which resulted in the lead and arsenic contamination of residential soils. Other soil characteristics which we did not measure, such as acidity, buffering capacity, organic content and $CaCO_3$ might also reduce bioavailability of the lead in soil (Chaney *et al.*, 1988).

Multiple potential sources of lead in the children's environment were identified. The make-up of a child's environment was found to be quite diverse and variable as a function of the child's age. It consisted of play areas in and around the home, relative's homes, day-care centers and neighbouring playgrounds. A comprehensive blood lead screening program consisting of a frequent blood sampling beginning early in life remains the best means of detecting children with increased lead intake irrespective of source. Once specific, at-risk children are identified, education, environmental monitoring and site-specific abatements can be used to reduce exposures.

The results of this environmental blood lead study provide important information to guide future blood lead screening in the community. First priority should be given to continued monitoring of those families already identified as having blood levels above the 10–15 $\mu g\ dL^{-1}$ level of concern. This should be coupled with focused educational efforts for those families and efforts to reduce clearly identified, significant lead sources in the family's immediate environment. Second priority should be given to screening families in the northern and western sections of the community, due to the greater frequency of occurrences of high paint lead and/or high soil lead concentrations. Ultimately all children less than 72 months of age should be screened once each year, with particular attention to children between the ages of 6 and 36 months. While abatement and education can play a role in reducing existing exposures, it is only through screening that some cases will be identified, *e.g.* a family which moves into the community subsequent to lead exposure in another community, a blood lead level elevation following plumbing work with lead solder, or the purchase and use of lead-glazed pottery.

The results of this study might also provide some insight into the expected change in blood lead levels following an intervention. For example, removal of soils above 2,000 ppm Pb and replacement with soils of 200 ppm would result in a new soil lead distribution. The effects of this change in soil lead on subsequent blood lead levels could be estimated from a statistical model. In doing so, the data are being used to make projections or forecasts. Numerous assumptions regarding the extent and effectiveness of abatements, the relative stability of other covariates and the role of secular trends must be made. Because of these limitations, forecasts can be extremely unreliable. The unreliability of forecasts can be even greater if the starting point is based on model-generated estimate of community blood lead levels rather than an actual epidemiological survey of community lead exposure. There are actually very few studies which provide direct evidence of the effectiveness of an abatement effort (see Charney *et al.*, 1983). Therefore, whenever a soil or dust abatement or remediation effort is planned, it would be very useful to obtain good environmental lead and blood lead data prior to and subsequent to the intervention. Only by this means can estimates be obtained of the short-term and long-term effectiveness of the intervention.

Conclusions

The average blood lead levels of children in the Midvale study area were found to be quite low (4.9 $\mu g\ dL^{-1}$). Three percent of the children exceeded 15 $\mu g\ dL^{-1}$; 12.7% exceeded 10 $\mu g\ dL^{-1}$. The average blood lead levels in pregnant women and nursing mothers were even lower (1.6 and 2.3 $\mu g\ dL^{-1}$). None exceeded 4.5 $\mu g\ dL^{-1}$. These levels are at or below current estimates for blood lead levels in non-exposed populations.

Lead-based house paint and lead contaminated soil were identified as the principle contributors to blood lead. The background blood lead in the absence of lead-based paint and lead contaminated soil was estimated to be about 4.0 $\mu g\ dL^{-1}$.

The effect of soil lead on blood lead was both small and weak. Blood lead was found to increase 1.25 $\mu g\ dL^{-1}$ per 1,000 ppm increase in lead in soil.

Location of residence was found to be a strong predictor of soil lead concentrations. Soil lead concentrations and blood lead concentrations were found to be the highest in the northern and western regions of the study area and lowest in the southeast quadrant of the study area. The difference in expected blood lead levels for the average child living in these two areas was small but statistically significant (5.9 *versus* 4.4 $\mu g\ dL^{-1}$).

Given the large and randomly selected study sample it is unlikely that the remaining 30% of Midvale children have blood lead levels which are statistically different from those tested.

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Urban Lead Exposures of Children in Cincinnati, Ohio

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Abstract

Environmental dust lead and other lead measures were highly intercorrelated for the wide range of housing in the Cincinnati prospective study. The causal pathway revealed by the data (soil and paint lead to surface dust lead to hand lead to blood lead) has been used to develop intervention strategies to reduce blood lead and hand lead levels which are currently being implemented in the Cincinnati Soil Lead Abatement Demonstration Project. These interventions, soil lead abatement, exterior dust abatement, and interior dust abatement, are being applied in various combinations in an examination of data for children residing in a single type of housing from birth. blood lead levels were compared according to three paint lead categories (low: < 2 mg cm^{-2}; medium: 2.1 to 6.0 mg cm^{-2}, and high: > 6.0mg cm^{-2}). Geometric mean blood lead values were 14.1 and 12.1 µg dL^{-1}, respectively, for the low and medium paint lead categories and much greater for children living in housing in the highest paint lead category, 24.8 µg dL^{-1}. These data suggest that for situations similar to those in Cincinnati, priority for lead-based paint abatement should be considered for the housing with paint lead above 6 mg cm^{-2}. A Ln–Ln relationship between environmental lead and blood lead for children in the Cincinnati study was found to represent the data much more closely than did a linear relationship such as that used in the current US EPA Lead Uptake/Biokinetic Model.

Introduction

About seven million tons of lead have been used in the USA in the past 100 years for white lead paint that was applied to the housing stock, primarily in the decades prior to the Second World War, and about an equal amount has been utilized as a gasoline additive, most of it in the 1950s through 1970s (US Bureau of Mines, 1989) (Figure 1). Children living in or in close proximity to older housing in large urban areas of the country, such as in portions of Cincinnati, Ohio, frequently have exposures to lead from residues from both of these sources. Although the introduction of new lead into the environment through both uses has been greatly reduced, lead exposures are still common both from environmental residues from former uses of each and from lead-painted surfaces that still exist on many of the homes that were built during the time period when lead-based paint was in common use. The Agency for Toxic Substances and Disease Registry has estimated that 42 million housing units throughout the nation occupied by approximately 12 million children still contain lead- based paint (1989). These and other children who live near or visit such homes are potentially exposed by contact with soil and dust that has previously been contaminated with residues from lead-based paint.

Soils and dusts became contaminated with lead-based paint that had been removed from painted surfaces by weathering and other auritional processes or that had been intentionally removed by scraping, solvents or by abrasive blasting. Similarly, soils and dusts near highways still contain some residues from automobile exhaust fallout during periods of time prior to the phase-out of the use of lead additives in gasoline. Gradually at least a portion of this lead contamination will be washed into gutters and sewers and thereby be transported to locations where the sewage treatment plant sludges and stream sediments are eventually deposited. It is estimated that 3,000 tons per year of lead enters the storm runoff from residential areas of US cities with populations greater than 100,000 (Pitt and Field, 1990).

Lead is also present in the environment from the many other uses for which it continues to be used, such as for storage batteries, cable covering, solder, *etc.* The major uses of lead in the USA from 1930 to 1988 are delineated in Table 1.

Recent analyses of environmental lead data from the prospective study of the effects of lead exposure on young children in Cincinnati (Bornschein *et al.*, 1985) will be presented in this paper. The interrelationships among the environmental lead levels, their association with housing of various ages and conditions, and their impact on blood lead will be presented.

Cincinnati Prospective Study

Since the early 1980s over 10,000 environmental lead measurements, consisting of paint, soil and dust samples and *in-situ* paint lead determinations, have been obtained for the housing of children participating in the Cincinnati longitudinal study of the effects of lead exposure on development. Over 80% of the approximately 5,000 samples collected for this study have now been analyzed.

Methods

Methods for collecting and analyzing interior and exterior dust, paint, and soil have been described elsewhere (Que Hee *et al.*, 1985). These environmental lead measures and their units are as follows: hand lead (µg Pb), interior surface dust (µg Pb g^{-1}

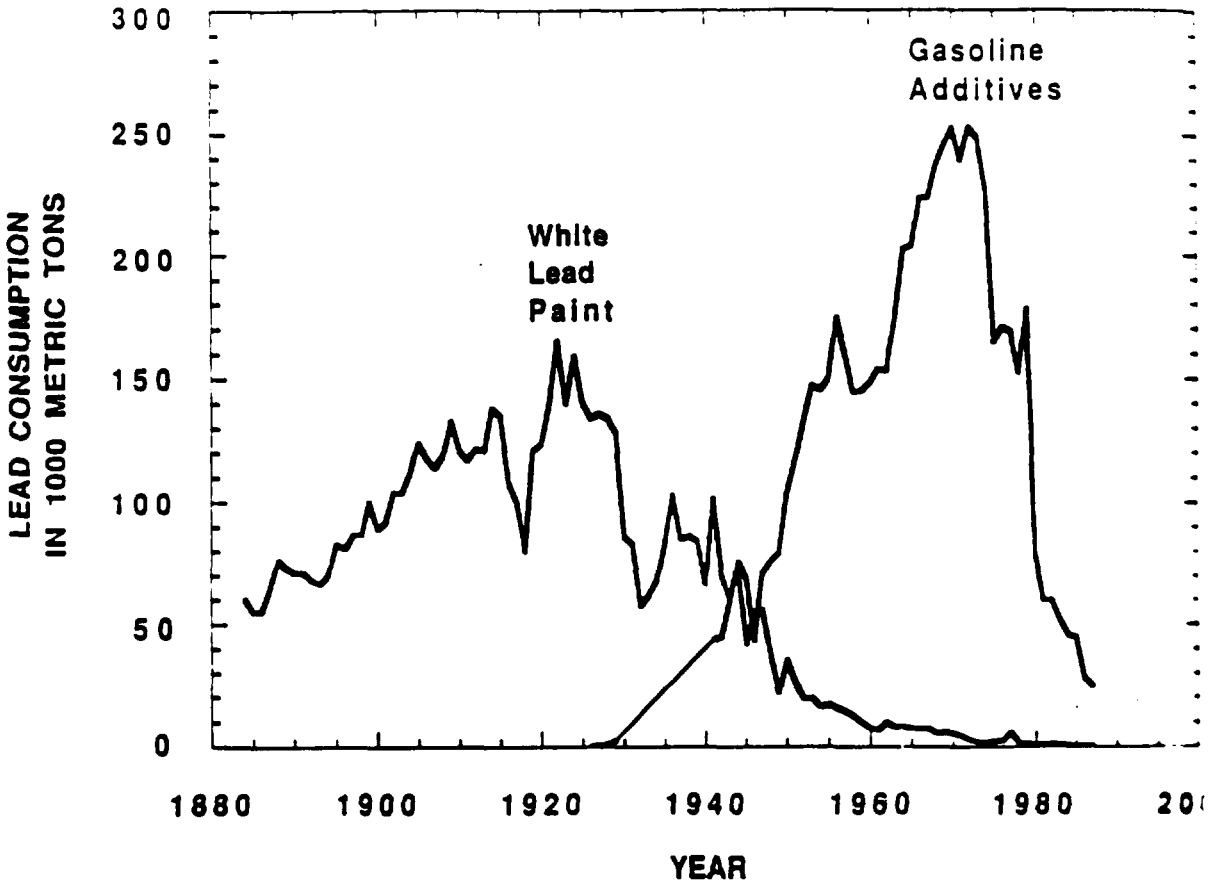


Figure 1 *United States lead consumption.*

Table 1 *Major uses of lead in the USA (percentage of total used).*

Use	1930	1940	1950	1960	1970	1980	1988
White lead	10.0	8.4	2.9	0.8	0.4	7.3[a]	5.1[a]
Red lead/litharge	4.2	7.6	8.2	7.3	5.7		
Gasoline additive	0.6	4[b]	9.2	16.0	20.5	12.0	2.3[b]
Storage batteries	21.2	28.2	32.2	34.6	43.6	60.3	77.6
Cable covering	27.1	13.7	10.7	5.9	3.7	1.3	1.3
Ammunition	4.3	7.2	3.1	4.3	5.3	4.5	4.3
Solder	3.5	3.1	7.6	5.9	5.1	3.9	1.5
Caulking	2.7	2.5	4.3	6.5	2.5	0.5	0.1
Total use (1,000 tonnes)	697	782	1123	926	1234	1073	1231

Source: Adapted from *US Minerals Yearbooks*, US Department of Interior, Washington, DC.

[a] Data not available separately.

[b] Estimated.

Table 2 *Environmental lead measures by housing type.*

Environmental lead measure[a]	Post-2nd WW private satisfactory condition	Public housing	Subsidized rehabilitated housing	19th century satisfactory condition private (non-rehab.)	19th century det./dilap.[b] (non-rehab)
Paint (ppm)					
Mean	[d]	2,750	2,820	30,500	25,200
(±1 SD)	–	(477–15,900)	(85–93,900)	(3,660–254,000)	(4,500–142,000)
n[c]	–	16	11	37	108
XRF (mg cm^{-2})					
Mean	1.2	1.7	1.2	7.3	10.5
(±1 SD)	(0.4–3.4)	(0.9–3.4)	(0.5–3.0)	(2.5–21.1)	(5.0–22.0)
n	51	112	111	92	163
Paint hazard[e]					
Mean	0.4	1.0	0.6	4.7	9.7
(±1 SD)	(0.1–1.4)	(0.4–2.4)	(0.2–1.7)	(1.2–19.1)	(3.2–29.0)
n	51	112	111	92	163
Interior surface dust (ppm)					
Mean	332	490	622	1,680	2,360
(±1 SD)	(151–733)	(242–996)	(289–1,340)	(586–4,800)	(957–5,840)
n	44	95	101	84	146
Interior surface dust (mg m^{-2})					
Mean	0.13	0.25	0.25	0.77	2.1
(±1 SD)	(0.04–0.43)	(0.09–0.72)	(0.07–0.93)	(0.13–4.72)	(0.46–9.50)
n	44	95	99	81	141
Interior dustfall (ppm)					
Mean	176	179	221	464	563
(±1 SD)	(55–567)	(53–612)	(67–727)	(136–1,590)	(174–1,820)
n	45	97	101	75	127
Interior dustfall(μg m^{-2}/30 days)					
Mean	0.035	0.054	0.075	0.139	0.199
(±1 SD)	(0.011–0.116)	(0.16–0.181)	(0.024–0.234)	(0.029–0.653)	(0.047–0.841
n	45	97	99	75	127
Exterior surface scraping (ppm)					
Mean	327	233	1,800	5,000	4,550
(±1 SD)	(118–905)	(87–622)	(611–5,280)	(1,430–17,500)	(1,180–17,600
n	21	67	81	45	96
Soil core (ppm)					
Mean	98	138	221	692	905
(±1 SD)	(37–264)	(67–284)	(59–826)	(259–1,840)	(384–2,130)
n	23	38	13	29	29
Hand Pb	subject (μg)				
Mean	4.3	4.8	7.5	10.5	15.5
(±1 SD)	(1.9–9.9)	(1.8–12.7)	(2.7–21.0)	(3.3–33.2)	(5.0–47.9)
n	44	98	96	83	143
Hand Pb	sibling (μg)				
Mean	7.4	7.2	13.2	15.3	24.4
(±1 SD)	(3.6–15.5)	(2.7–19.6)	(4.9–35.7)	(5.1–45.8)	(8.2–72.7)
n	18	42	52	41	84

[a] Median values per housing unit used in the analysis of paint, surface dust, scraping, soil core and sibling hand lead data; for XRF the max. of 15 values per household was used. Geometric means and standard deviations for all housing unit environmental measures are shown.

[b] Det./Dilap. refers to housing in deteriorated or dilapidated condition as determined by exterior evaluation (Clark, 1985).

[c] *n* – number of housing units.

[d] Fewer than 10 values analyzed.

[e] Paint hazard is a measure which includes the XRF value of a surface with a qualitative measure of the extent to which the paint is loose and therefore potentially available to a child.

Table 3 Intercorrelations among environmental lead measures[a]

Environ. Pb measure		Interior surface dust		Interior dustfall		Exterior dustfall		Exterior surface dust	Soil core	Hand lead
	XRF ($mg\ cm^{-2}$)	(ppm)	($mg\ m^{-2}$)	(ppm)	($mg\ m^{-2}$ /30 days)	(ppm)	($mg\ m^{-2}$ /30 days)	scraping (ppm)	(ppm)	Subject
Paint (ppm)										
r[b]	0.33	0.32	0.29	0.12	0.16	0.14	-0.11	0.30	0.30	0.190
p	0.0001	0.0001	0.0001	0.13	0.05	0.6	0.7	0.0005	0.04	0.01
n	188	181	176	153	153	19	19	130	45	175
XRF[c] ($mg\ cm^{-2}$)										
r		0.63	0.51	0.40	0.42	-0.25	-0.18	0.49	0.53	0.32
p		0.0001	0.0001	0.0001	0.0001	0.02	0.3	0.0001	0.0001	0.0001
n		512	502	485	483	33	33	33	149	495
Interior surface dust (ppm)										
r			0.72	0.36	0.43	0.32	0.29	0.60	0.53	0.45
p			0.0001	0.0001	0.0001	0.07	0.1	0.0001	0.0001	0.0001
n			503	431	429	33	33	330	149	474
Interior surface dust ($mg\ m^{-2}$)										
r				0.30	0.33	0.10	0.17	0.45	0.44	0.36
p				0.0001	0.0001	0.6	0.3	0.0001	0.0001	0.0001
n				423	421	33	33	326	145	464
Interior dustfall (ppm)										
r					0.73	0.00	-0.03	0.38	0.32	0.30
p					0.0001	1.0	0.9	0.0001	0.0002	0.0001
n					488	32	32	288	134	421
Interior dustfall ($mg\ m^{-2}$/30 days)										
r						-0.07	0.06	0.44	0.40	0.33
p						0.7	0.7	0.0001	0.0001	0.0001
n						32	32	286	134	419
Exterior dustfall (ppm)										
r							0.89	0.22	0.36	0.27
p							0.0001	0.3	0.3	0.1
n							33	25	9	33
Exterior dustfall ($mg\ m^{-2}$/30 days)										
r								0.14	0.67	0.37
p								0.5	0.05	0.04
n								25	9	33
Exterior surface dust scraping (ppm)										
r									0.60	0.36
p									0.0001	0.0001
n									104	314
Soil core (ppm)										
r										0.30
p										0.0003
n										144
Hand lead subject (μg)										
r										
p										
n										

[a] Median values per housing unit used in the analysis of paint, surface dust, scrapings, soil core and sibling hand lead d
[b] Pearson r.
[c] Maximum value obtained from 15 locations per residence used in analysis.

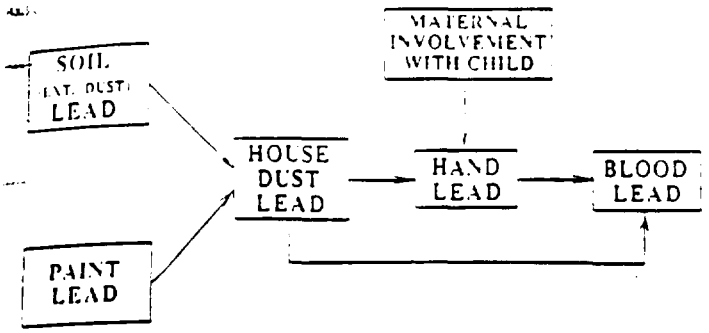


Figure 2 *Child lead exposure model.*

dust and μg Pb m^{-2}), interior and exterior dustfall (μg Pb g^{-1} dust and μg Pb m^{-2} per 30 days), exterior surface scrapings (μg Pb g^{-1} dust), and one-inch soil cores (μg Pb g^{-1} soil).

Paint lead is determined by two methods: *in-situ* X-ray fluorescence method (mg Pb cm^{-2}) and by laboratory chemical analysis of paint chips (μg Pb g^{-1} paint). A qualitative measure of condition of painted surface is also combined with the XRF value to yield a paint hazard score. Each set of data from an environmental visit typically consists of results from *multiple* samples for many of the environmental lead measures such as paint, interior surface dust, sibling hand lead, soil cores and exterior surface scrapings. Median values per housing unit are used in the analysis of all of these measures except XRF data for which the maximum of the 12–15 measurements usually collected for each house is used because it had slightly better predictive value than the median. Housing type is determined by an exterior qualitative evaluation (Clark *et al.*, 1985) which categorizes the housing into five major categories: post Second World War housing in satisfactory condition, public housing, subsidized rehabilitated housing, twentieth century non-rehabilitated housing in satisfactory condition and nineteenth century non-rehabilitated housing in deteriorated or dilapidated condition. The rehabilitated housing had previously undergone thorough 'gut' rehabilitation, mainly in the 1970s, that effectively replaced almost all of the interior painted surfaces with new material and the paint was removed from most exterior surfaces by sandblasting or chemical stripping.

Table 4 Correlations between hand lead and paint lead or interior dust as a function of child's age.

Child's age (months)	n^a	Paint[b] hazard	Interior dust (ppm)	Interior dust (mg m^{-2})
6	190	0.35	0.35	0.38
12	223	0.35	0.38	0.39
18	225	0.30	0.40	0.34
24	189	0.28	0.38	0.29
30	180	0.32	0.39	0.22 (0.003)
36	159	0.33	0.47	0.31
42	142	0.35	0.50	0.32
48	128	0.24 (0.004)	0.44	0.32 (0.0002)
54	112	0.22 (0.01)	0.39	0.29 (0.002)
60	90	0.16 (0.1)	0.36 (0.0005)	0.26 (0.01)

Correlations significant at $p = 0.0001$ unless shown.
[a] Minimum
[b] Paint hazard is a measure which includes the XRF value of a surface with a qualitative measure of the extent and manner in which the paint is failing and therefore potentially available to a child.

Results

Geometric mean values for the environmental lead measures by housing type and ranges (± 1 standard deviation) (Table 2) indicate wide ranges and differences in levels depending upon

Table 5 *Correlations between blood lead and paint lead, interior dust or hand lead as a function of child's age.*

Child's age (months)	n^a	Paint[b] hazard	(ppm)	Interior dust (mg m^{-2})	PbH
6	196	0.32	0.14 (0.04)	0.25 (0.0004)	0.33
12	234	0.43	0.42	0.42	0.51
18	235	0.43	0.41	0.37	0.44
24	196	0.36	0.44	0.39	0.44
30	186	0.25 (0.0003)	0.42	0.37	0.45
36	167	0.15 (0.03)	0.41	0.48	0.46
42	150	0.20 (0.006)	0.35	0.41	0.51
48	137	0.11 (0.15)	0.20 (0.016)	0.24 (0.004)	0.43
54	125	0.16 (0.04)	0.30 (0.0007)	0.29 (0.001)	0.40
60	98	0.05 (0.5)	0.23 (0.02)	0.27 (0.006)	0.48

Correlations significant at $p = 0.0001$ unless shown.
[a] Minimum.
[b] Paint hazard is a measure which includes the XRF value of a surface with a qualitative measure of the extent and manner in which the paint is failing therefore potentially available to a child.

Table 6 *Lead exposure, blood lead and housing for groups of children divided by lifetime average [illegible] for children residing in a single type of housing from birth (n = 153).*

	Arithmetic means			
	1st (low)	2nd	3rd	4th (high)
	29	39	44	41
$XRF_{MAX\ INT}$ (mg cm^{-2})	3.0	2.9	4.7	10.8
$XRF_{MAX\ EXT}$ (mg cm^{-2})	1.1	4.9	7.6	12.1
Pb $Dust_{INT}$ (μg g^{-1})	1,070	955	1,500	2,370
Pb $Soil_{SURFACE}$ (μg g^{-1})	2,540	1,960	5,830	6,830
SES	16.6	19.2	17.8	15.4
$PbB_{18\ MO}$ (μg g^{-1})	9.0	12.0	16.6	27.3
% $PbB_{18\ MO}$ > 15 (μg dL^{-1})	7	13	55	95
% $PbB_{18\ MO}$ > 25 (μg dL^{-1})	3	0	7	46
% 19th century deteriorated	7	8	18	59
% Rehabilitated	31	31	41	22
% Public	52	44	18	7
% 19th century satisfactory	7	8	20	12
% Other	3	9	3	0

$XRF_{MAX\ INT}$ = Mean of maximum X-ray fluorescence determination of interior paint lead.
$XRF_{MAX\ EXT}$ = Mean of maximum X-ray fluorescence determination of exterior paint lead.
Pb $Dust_{INT}$ = Interior surface dust.
Pb $Soil_{SURFACE}$ = Exterior surface scrapings of soil/dust.
$PbB_{18\ MO}$ = Blood lead level of 18-months old children.

housing type. Lowest levels occurred in the post-Second World War private satisfactory housing and in public housing, and highest values for the nineteenth century non-rehabilitated housing in deteriorated or dilapidated condition and intermediate for the nineteenth century rehabilitated housing and non-rehabilitated satisfactory housing. For paint lead analyzed by XRF, the rehabilitated housing had somewhat lower values than the public housing, reflecting the fact that the rehabilitation occurred somewhat later (primarily 1970s) than the construction of the public housing (primarily 1930s through 1960s). For the older housing types (rehabilitated housing and the other nineteenth century housing) dust lead concentrations (μg g^{-1}) were lowest for interior dust/all with interior surface dust being intermediate and exterior surface scrapings being highest.

If one assumes that the dust on the children's hands has the same mean lead concentration as the interior surface dust then the average *quantity* of dust on the hands of the children's hands would be 9.6 mg, with a range by housing type from 6.3 to 13.0. If the average surface area of the children's hands were known, then hand lead could also be expressed as mg Pb m^{-2} of hand surface area. Using an estimate of 0.040 m^2 for the surface area of the hands of 3 to 4-year old male children (US EPA, 1989), the geometric mean hand lead on a mg Pb m^{-2} basis would therefore be 0.27 and ranging by housing type from 0.11 (post Second World War housing) to 0.39 (nineteenth century, det./dil.), following a pattern resembling that for interior dust. These surface loadings on hands are remarkably similar to those for interior dust except that the range by housing category is only one-fourth as high.

The environmental lead measures were highly

Table 7 *Environmental lead and blood lead level lead category for children residing in a single typ housing from birth (mg Pb cm^{-2}) (n = 153).*

	Arithmetic	
	< 2.0	2.1-4
n	85	24
$XRF_{MAX\ INT}$ (mg cm^{-2})	1.2	3.1
$XRF_{MAX\ EXT}$ (mg cm^{-2})	1.4	7.2
Pb $Dust_{INT}$ (μg g^{-1})	805	1540
Pb $Soil_{SURFACE}$ (μg g^{-1})	1940	2720
SES	17.7	16.5
$PbB_{18\ MO}$ (μg dL^{-1})	14.1	12.1
% $PbB_{18\ MO}$ > 15 (μg dL^{-1})	34	29
% $PbB_{18\ MO}$ > 25 (μg dL^{-1})	7	0
% 19th century deteriorated	2	21
% Rehabilitated*	53	8
% Public	33	63
% 19th century satisfactory	7	8

$XRF_{MAX\ INT}$ = Mean of maximum X-ray fluores determination of interior paint lead.
$XRF_{MAX\ EXT}$ = Mean of maximum X-ray fluores determination of exterior paint lead.
Pb $Dust_{INT}$ = Interior surface dust.
Pb $Soil_{SURFACE}$ = Exterior surface scrapings of so
$PbB_{18\ MO}$ = Blood lead level of 18-months old ch

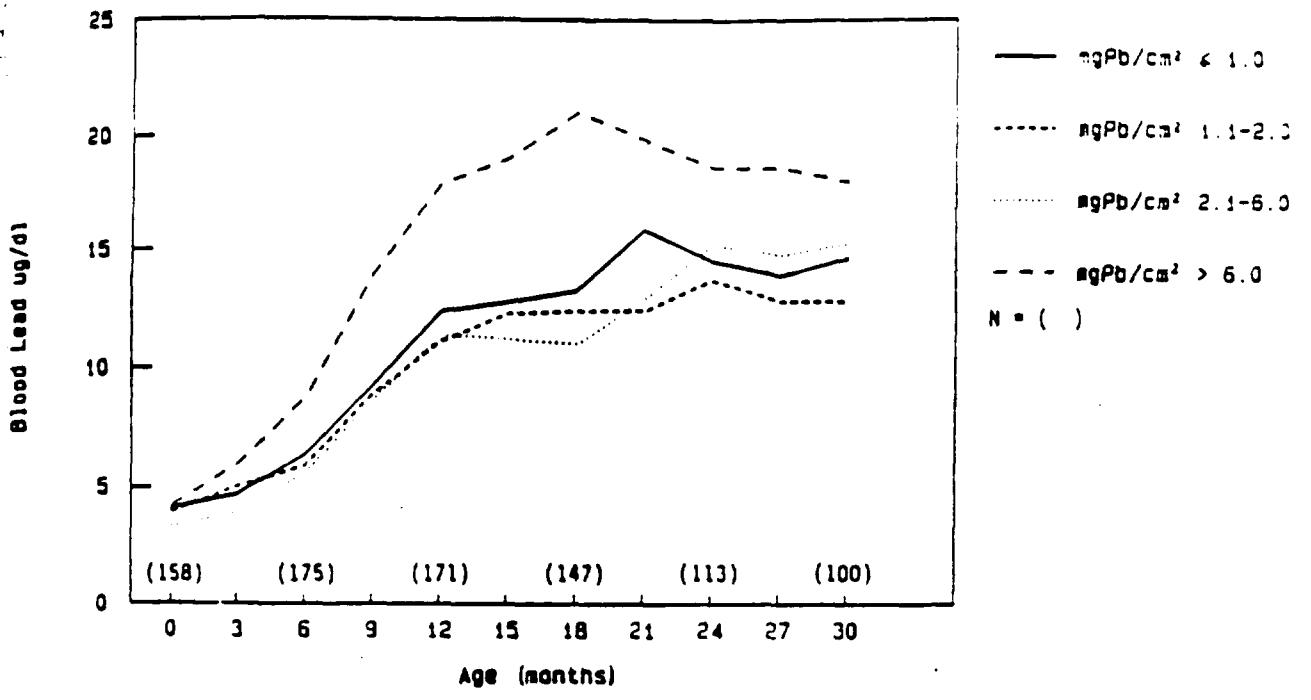


Figure 3 *Effect of lead in paint on blood lead.*

intercorrelated (Table 3). The highest r values were associated with the correlations between the mass concentration ($\mu g\ g^{-1}$) of the interior surface dust measure and the dustfall measures and their corresponding area loading ($\mu g\ m^{-2}$ and $\mu g\ m^{-2}$per 30 days, respectively) where r values ranged from 0.72 to 0.89 ($p \pm 0.0001$).

For 18-month old children an analysis of the environmental and blood lead data by an approach known as structural equations modeling revealed a predictive exposure pathway showing the interrelationships among the various behavioral and environmental measures leading to elevations in blood lead (Figure 2). This pathway showed an influence of exterior surface scraping level and paint hazard on interior surface dust, which in turn influenced hand lead; hand lead level and a behavioral measure (maternal involvement with child) were then predictive of blood lead. A similar model has been developed for mining, milling and inactive smelting areas (Bornschein *et al.*, 1988, 1990). These models lead to the conclusion that if exterior surface dust lead level, presumably a surrogate for paint lead concentration and soil contaminated by various sources, were reduced, then the blood lead level would also be reduced. A simultaneous reduction in interior dust lead would presumably hasten the reduction in blood lead. These implications are currently being tested in the Cincinnati Soil Lead Abatement Demonstration Project (Clark *et al.*, 1988).

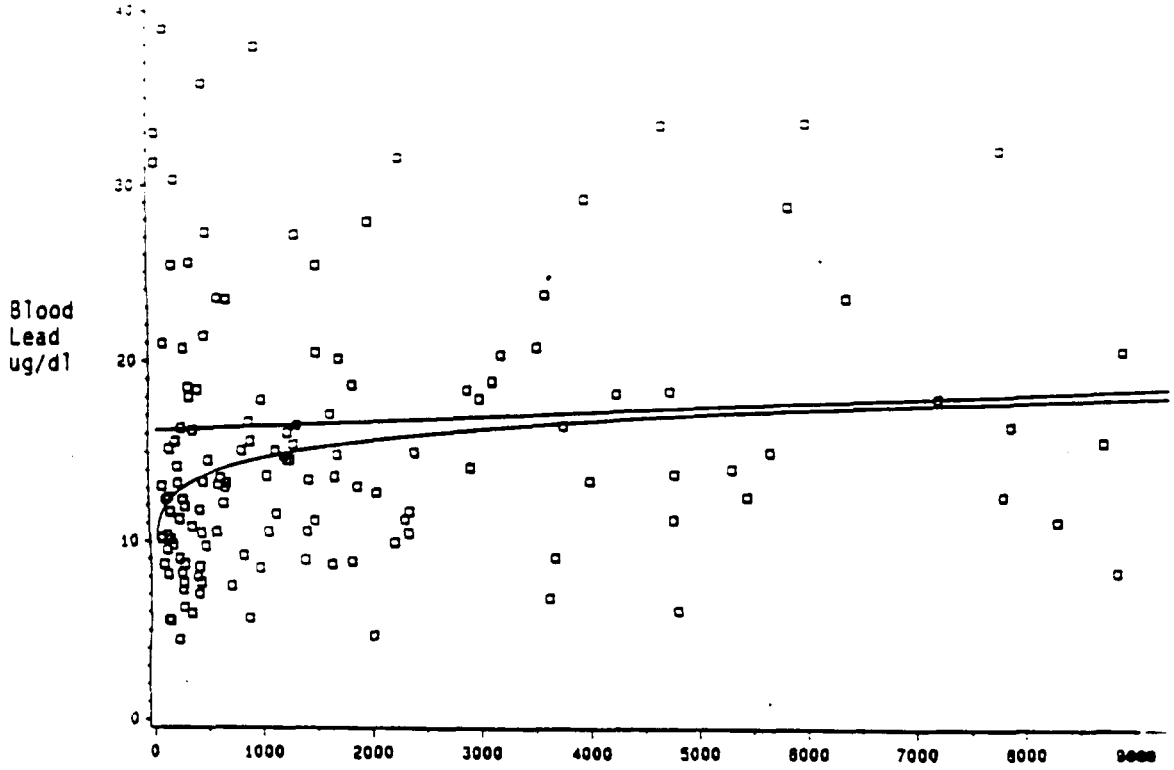
Bivariate correlations between hand lead and paint hazard or interior surface dust (Table 4) as a function of age of child show statistically significant relationships from 6 months of age to 60 months of age for interior dust and to 54 months for paint hazard. The correlation is higher for interior dust expressed on a mass concentration basis ($\mu g\ g^{-1}$) than on an area loading basis ($\mu g\ in^{-2}$), except at 6 and 12 months, and appears to peak at 42 months. Correlations between blood lead and paint [illegible] interior surface dust and hand lead (Table [illegible] significant correlations (ranging from 0.15 to 0.5[illegible] 60 months except for paint lead for which the correlation was significant only up to 42 months of age.

Environmental and Social Variables by Blood Lead Quartile

For the 153 children who have resided in a single housing type from birth, examined by blood lead quartile, the values for selected environmental, social and blood lead variables are shown in Table 6. Housing type differed greatly among the quartiles with the percentage of children in the quartile living in 19th century dilapidated/deteriorated housing being 59 for the highest quartile and only 7 and 8 for the two lower quartiles. The percentage of children in the quartile residing in rehabilitated and public housing decreased from 83 for the lowest quartile to 29 in the highest blood lead quartile. Exterior paint lead values (XRF) increased gradually from the low to the high quartile but interior values did not differ between the two lower quartiles. Interior surface dust lead levels were similar for the two lower quartiles and then increased for the higher two. Exterior surface soil (scrapings) were lower for the second than the lowest quartile and were increased considerably for the higher two quartiles. SES was similar for all four quartiles.

Blood Lead by Paint Lead Category

For the same children residing in a single housing type, as shown in Table 6, blood lead, housing type and selected other factors are presented in Table 7. An interesting feature of these



		R^2	
Ln-Ln	$\ln(Pb8_{18}) = 2.055 + .092 \ln (PbS)$	.084	.4
Linear	$Pb8_{18} = 16.22 + .00026\ PbS$	.037	.4

($Pb8_{18}$ refers to blood lead level of 18-month old children)

Figure 4 *Blood lead as a function of exterior surface scraping (Ln–Ln and linear).*

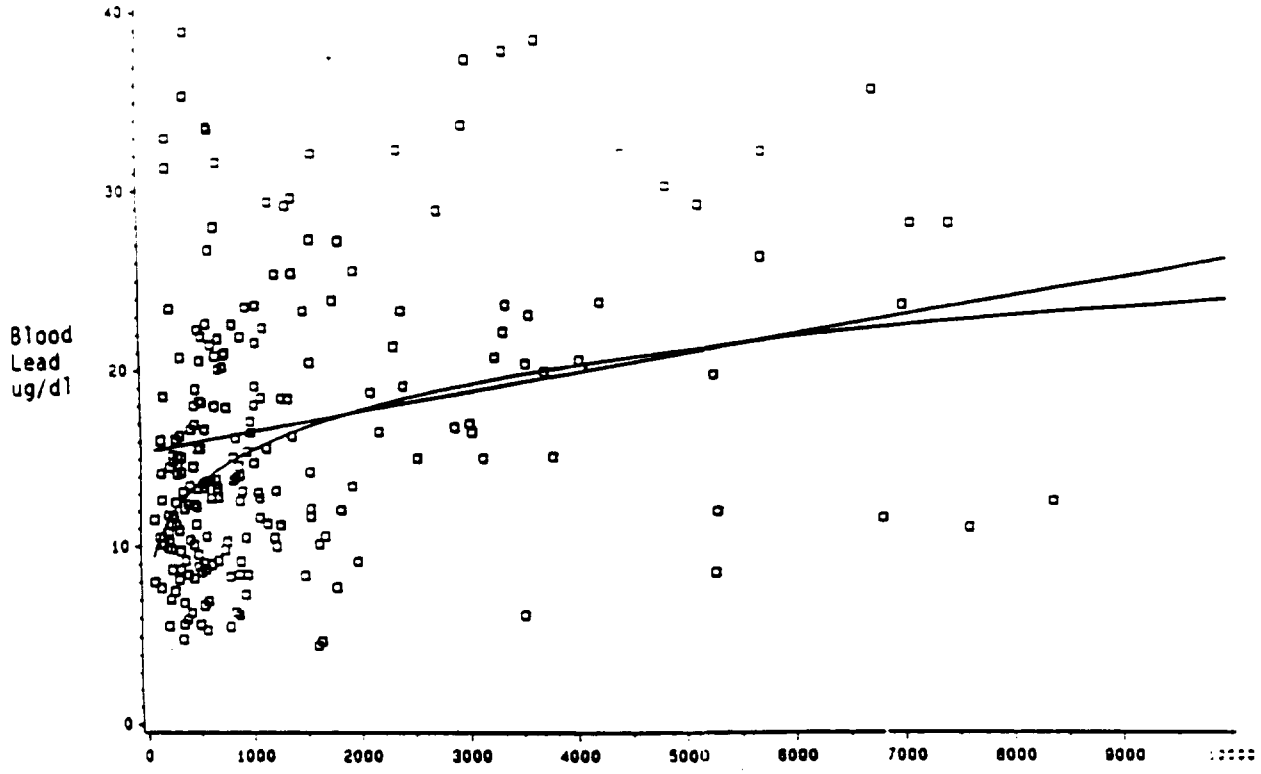
results is that blood lead levels do not differ between the lower two of the three paint lead categories (less than or equal to 2.0 mg cm^{-2} and between 2.1 and 6.0 mg Pb cm^{-2}), for which average blood lead values were 14.1 and 12.1 $\mu g\ dL^{-1}$, respectively. The percentage of the children living in rehabilitated and public housing ranged from 86 in the lower paint lead category to 2.0 in the highest category, > 6.0 mg Pb cm^{-2}. Graphically, blood lead level by paint lead level are also shown in Figure 3. These data suggest that priority should be given to the abatement of paint in urban housing where lead levels exceed 6 mg cm^{-2}.

Linear and Ln–Ln Correlations of Blood Lead and Soil/Dust Lead

The Lead Uptake/Biokinetic Model that is being developed by the US EPA for the prediction of the blood lead level of children assumes linear relationships between blood lead and environmental lead measures such as soil and dust lead concentration. Regression equations for soil (surface dust scrapings) *versus* blood lead and for dust lead *versus* blood lead were determined for the Cincinnati data for both Ln–Ln and linear relationships and are presented in Figures 4 and 5, respectively. Substantial differences exist in predictions of blood lead from these two models, particularly for soil and dust lead concentrations below 2,000 ppm. For ea increase in exterior surface scraping lead conc 500 to 1,000 ppm, the linear model predicts increase of 0.07 $\mu g\ dL^{-1}$, or 0.14 $\mu g\ dL^{-1}$ p increase in lead concentration. The Ln–Ln model increase in exterior surface scraping concentra blood lead increase of 0.91 $\mu g\ dL^{-1}$ or 1.82 1,000 ppm increase or 13 times that predicted equation. For the Cincinnati data, the Ln–Ln mo a much better fit, especially for exterior surface l interior dust lead levels below about 2,000 $\mu g\ g$

Summary

The dust pathway appears to be a major one fo lead by young children both in older urban areas mining areas in the USA, with interior surface du predictive of hand lead which in turn predict Interior dust lead level is influenced by lead l exterior to the housing unit such as in exterior sur Interior and exterior dust lead levels in Cincinn greatly influenced by the type of housing involve are highest for housing built in the nineteenth ce poor state of maintenance and repair. A major inc lead has been observed for children residing in l



		R^{12}	n	
Ln-Ln	$\ln(Pb8_{18}) = 1.4190 + .192 \ln(PbD)$	.165	235	<
Linear	$Pb8_{18} = 15.482 + .0011\ PbD$	.109	235	<

($Pb8_{18}$ refers to blood lead level of 18-month old children)

Figure 5 *Blood lead as a function of interior dust (Ln–Ln and linear).*.

the paint lead level, on a mg Pb cm^{-2} basis, is above 6.0, when compared with blood lead in children living in housing with lower paint lead levels. Little if any difference in blood lead levels was observed for children residing in housing with paint lead levels from 0 to 2.0 mg cm^{-2} and between 2.1 and 6.0 mg cm^{-2}. These observations suggest that for inner-city areas similar to those in Cincinnati consideration should be given to assigning a lead-paint-abatement *priority* to those housing units in low-income areas where paint lead levels are above 6.0 mg Pb cm^{-2} and found to be in poor condition.

Acknowledgments

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Relationship Between Soil Lead Levels and Blood Lead Levels Among Children Living Near a Lead Smelter in Jamaica*

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Abstract

A survey was conducted to determine the distribution and determinants of environmental and blood lead levels near a conventional and several cottage lead smelters and to assess the relationship between environmental and blood lead levels in a tropical, developing-country setting. Fifty-eight households were studied in the Red Pond community, the site of the established smelter and several backyard smelters, and 21 households were studied in the adjacent, upwind Ebony Vale community in Saint Catherine Parish, Jamaica. Elevated levels of lead in soil and housedust and elevated blood lead levels in children were largely confined to the Red Pond community. In that community, soil lead was the strongest predictor of PbB among Red Pond subjects under 12 years of age. The blood lead–soil lead relationship in children differed from that reported in developed countries; blood lead levels were higher than expected for the household- specific soil lead levels that were observed.

Introduction

Lead poisoning associated with conventional lead smelting in developed countries has been described among both workers (Lilis *et al.*, 1977) and community residents (Popovac *et al.*, 1982; Landrigan *et al.*, 1975; Brunckreef *et al.*, 1981). While airborne lead fume from smelters is the main vehicle of environmental contamination, the most important route of community lead exposure in such settings appears to be ingestion of lead- contaminated soil and housedust, especially by children (Roels *et al.*, 1980). Children of smelter workers may be at particularly high risk from exposure to lead dust brought home on work clothes (Morton *et al.*, 1982; Baker *et al.*, 1977).

The relationship between environmental lead contamination and blood lead levels in children has been extensively studied (Duggan and Inskip, 1985), and data from such studies have been used to propose 'maximum permissible levels' of lead in soil (Madhavan *et al.*, 1989). However, nearly all previous studies have been carried out in developed countries with temperate climates. Because unintentional soil and dust ingestion may be related to hygiene and to time spent outdoors (Duggan and Inskip, 1985), and because lead absorption is influenced by nutrition (Mahaffey, 1982), one might expect soil lead – blood lead relationships to differ in tropical, developing countries.

Cottage lead smelters are scattered throughout Jamaica. The clustering of several of these so-called 'backyard' lead smelters in a community near a conventional, secondary lead smelter provided the opportunity to assess, during a cross-sectional survey conducted in October, 1987, the amount of environmental contamination associated with both cottage and conventional smelting in the same community. In addition, the relationship between environmental contamination and blood lead levels in a tropical, developing country was examined. A complete report of this survey has been reported previously (Matte *et al.*, 1991); this paper summarizes the findings concerning soil lead exposure and blood lead levels in children.

Study Site and Methods

The conventional lead smelter ('established smelter') has operated at the southeast corner of the Red Pond Road community (estimated population 2,500) since 1963, reclaiming lead from spent car batteries. The smelter, which usually operated for about two weeks out of every two month period, did not operate during the several weeks before or during the

* This paper summarizes a previously published report (Matte *et al.*, 1991)

Table 1 *Households and children enrolled, community lead survey, Jamaica, October 198[illegible]*

Selection criteria	Red Pond: Possible backyard smelter	Red Pond: Random sample	Ebony Vale: Random sample
Households			
No. participating (% of those sampled)	9 (100)	49 (86)	21 (68)
Mean household size	5.3	7.6	4.4
Mean household income (US$/week)	32	42	93
Children tested for blood lead, by age (% of eligible children in participating households)			
6 months–5 years	8 (100)	57 (93)	16 (84)
6–11 years	9 (90)	53 (88)	14 (82)

Table 2 *Environmental lead levels and blood lead levels in children at survey.*

Measurement		Red Pond: Possible backyard smelter	Red Pond: Random sample	Ebony Vale: Random sample
Pb soil–area (ppm) GM		1,089*	133***	6
	% ≥ 500 ppm	75[a]	24[b]	0[a]
Pb soil–peak (ppm) GM		7,691**	221***	7
	% ≥ 500 ppm	89	27	0
Pb dust ($\mu g\ m^{-2}$) GM		2,790*	690***	100
	% ≥ 1,500 $\mu g\ m^{-2}$	56	24[b]	0[a]
Blood Pb ($\mu g\ dL^{-1}$), by age:				
≤ 5 years GM		25[ns]	21***	9
	% ≥ 25 $\mu g\ dL^{-1}$	50	44	0
6–11 years GM		62***	17***	7
	% ≥ 25 $\mu g\ dL^{-1}$	100	40	7

[a] Missing for 1 household.
[b] Missing for 3 households.
GM geometric mean.
[ns] not significant.
p values for differences in geometric means, possible backyard smelter compared with randomly-selected Red Pond households, and randomly-selected Red Pond Households compared with Ebony Vale households: *, $p < 0.05$; **, $p < 0.005$; ***, $p < 0.0005$.
$\mu g\ dL^{-1}$ = micrograms per deciliter of whole blood. ppm = parts per million.

survey. Several crude backyard lead smelters are also known to operate in this relatively poor community, and some residents have reportedly used lead oxide-containing drums and dross (slag) from the established smelter grounds for fencing and landfill material. A middle-class housing development, known as Ebony Vale (estimated population 1,600), had been recently completed just east of the conventional smelter. Prevailing winds in the area come from the northeast. Lead poisoning cases have been recognized in Red Pond but not in Ebony Vale.

Potential study households were sampled within Red Pond and Ebony Vale from community survey maps. In addition, all households in Red Pond reported by established smelter employees to be at, or adjacent to, backyard smelter surveyed. Blood lead measurement was offered for a[illegible] of surveyed households who were at least six mont[illegible] Most non-participants were not at home when the d[illegible] surveyed. The results of household and subject sel[illegible] summarized in Table 1.

At each participating household, a question[illegible] administered to a responsible adult who provided de[illegible] and behavioral information about each household r[illegible] one centimeter deep core soil sample in the approxim[illegible] of the yard was collected. Lead (Pb) levels in such sa[illegible] be referred to as 'Pb soil–area'. Soil was also sam[illegible]

Table 3 *Correlation coefficients (r) between log10-transformed environmental lead and blood lead levels of children in the Red Pond community.*

	Pb soil–area	Pb soil–peak	Pb dust
Blood lead levels, by age[a]			
≤ 5 years (N = 62)	0.75***	0.74***	0.57***
6–11 years (N = 52)	0.71***	0.69***	0.37

[a] only includes children in households with no missing environmental levels.
p values for correlation coefficients: ***, $p < 0.0005$.

Table 4 *Multiple regression models of log-transformed blood lead among children in the Red Pond community*

Age group	Independent variables	Parameter estimate	SE	Y intercept	Model r^2	
≤ 5 years	Pb soil–area (ppm)[a]	0.27	0.03	0.63	0.68	
	% of yard covered by exposed soil	0.0025	0.0005			
	Direction from smelter stack[b]					
	North-northwest	0.16	0.08			
	East	0.20	0.08			
	Southwest	–0.12	0.08			
6–11 years	Pb soil–area (ppm)[a]	0.31	0.03	0.58	0.51	

[a] Log-transformed.
[b] In assigning 'sectors' of direction from the established smelter stack the northeast and southeast quadrants were combined because of small numbers and similar environmental lead levels. The northwest quadrant was divided into sectors because most study households were in that quadrant. The west-northwest sector was the referent category.

potential sources of lead contamination, such as oxide drum fencing or lead scrap. The highest soil lead found in each yard will be referred to as 'Pb soil–peak'. The proportion of each yard covered by bare soil was estimated by observation. Dust samples were collected, using a published procedure (Vostal *et al.*, 1974), from the center of the floor in the room where children spend the most time. Scrapings of housepaint were taken at households where peeling paint was observed. Blood samples were obtained by venipuncture.

Lead levels in whole blood were measured by anodic stripping voltammetry (Searle *et al.*, 1973) by a reference laboratory in the Centers for Disease Control (CDC), Health Resources and Services Administration, Wisconsin State Laboratory of Hygiene Proficiency Testing Program. The limit of quantitation was 5 μg dL^{-1}. Every twentieth sample was split and analyzed by the CDC Nutritional Biochemistry Laboratory. The split sample results obtained by the study laboratory correlated well with the CDC results ($r = 0.99$) with a slope of 0.997 and intercept not significantly different from zero. Lead levels in environmental samples were measured by an American Industrial Hygiene Association accredited laboratory using inductively coupled plasma atomic emission spectroscopy (National Institute for Occupational Safety and Health, 1984). Limits of quantitation were 5 ppm for lead in soil, .24 μg m^{-2} for lead in dust, and 0.01% for lead in paint. Soil samples spiked with known additions of lead were analyzed in blinded fashion, with an estimated recovery slope of 0.947 of the amount added.

Continuous variables were transformed to correct skewness in distributions and apparent non-linear relationships between variables. T-tests and ordinary least squares regressions were used to analyze environmental lead data. To assess the any tendency of blood lead values to cluster within households, blood lead data were analyzed using statistical programs (Shah, 1981; Holt, 1982) that employ a Taylor series approximation to compute standard errors of estimated means and regression coefficients using households (rather than individuals) as sampling units.

Results

Geometric mean Pb soil–area, Pb soil–peak, and Pb dust were 22, 31, and 7 times, respectively, higher in Red Pond than Ebony Vale ($p < 0.0005$, Table 2), where the highest soil lead level was 150 ppm. Fourteen Ebony Vale households had Pb soil–area levels below 5 ppm. Soil lead levels were significantly higher at possible backyard smelter households than at other Red Pond households ($p < 0.005$). Differences in children's blood lead levels among the three groups showed a similar pattern to the levels of lead in soil and housedust.

The soil and dust levels in Ebony Vale, being low and quite uniform, were not significantly correlated with blood lead levels in that community, and the analyses reported below are limited to the Red Pond community. Analyses of predictors of blood lead within Red Pond included those 114 children for which corresponding soil lead and housedust lead values were not

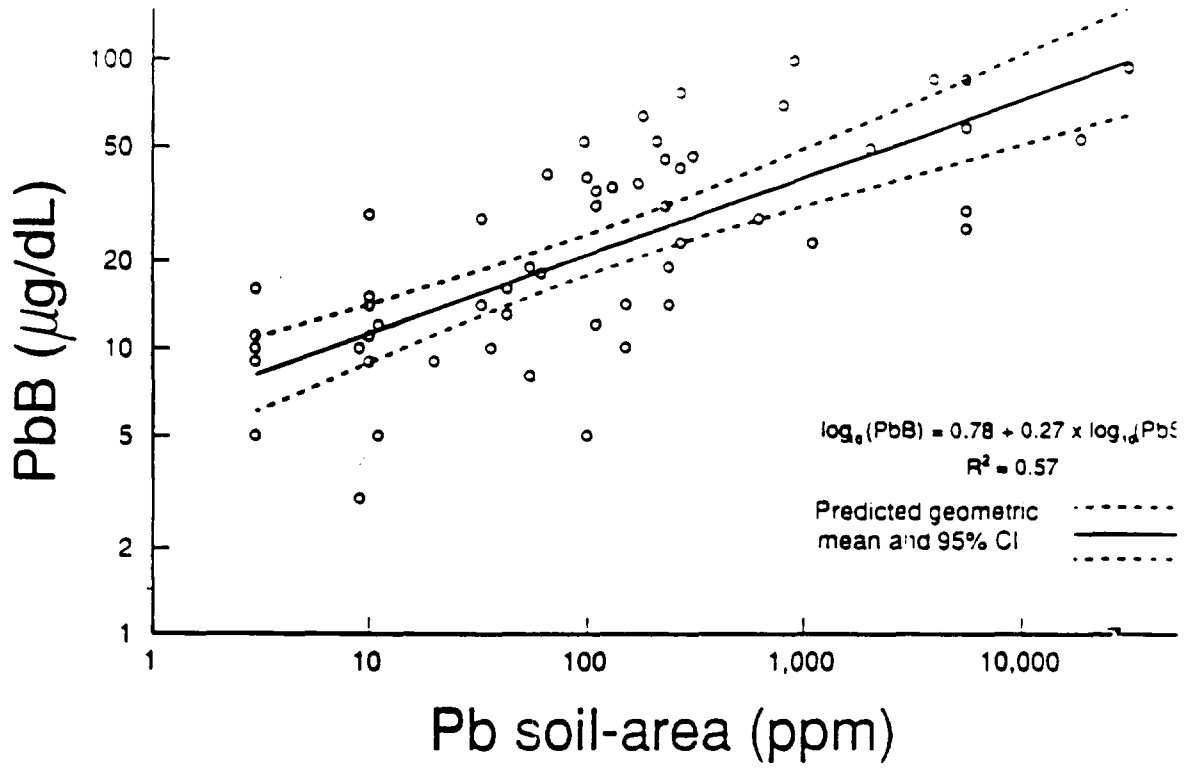

Figure 1 *Relationship between area soil lead (Pb) and blood lead (PbB) among children less than six years of ... Pond community.*

missing. Among both pre-school and school-aged children, blood lead was more strongly correlated with soil lead than with dust lead (Table 3). The relationship with soil lead was strongest among children under 6 years of age (Figure 1).

In separate multiple regression analyses for each age group, backwards elimination was used to arrive at the minimum set of variables best predicting blood lead. Starting models included soil, dust, and paint lead levels, distance and direction from the smelter stack, distance to a backyard smelter, presence of a lead worker in the household, portion of yard covered by bare soil, sex, household income, frequency of play near a smelter, pica, time unattended by an adult, and age. The least statistically significant predictors by partial F tests were dropped until only those significant at the $p < 0.05$ level remained. Final models are shown in Table 4.

Discussion

Lead contamination in the Red Pond Community is related, in part, to a contamination source well-documented elsewhere: conventional, secondary lead smelting (Landrigan *et al.*, 1975; Brunckreef *et al.*, 1981; Roels *et al.*, 1980). A less familiar cottage industry, 'backyard' lead smelting, also causes high level lead exposure for nearby residents. While the efficiency of the backyard smelting process has not been formally studied, such operations may reclaim as little as 30% of the lead in scrap; much of the remainder is discarded in heavily-contaminated dross skimmed from the molten lead. In addition to fallout from lead fume generated by smelting, lead contamina spread by lead dust that is blown or tracked from p or lead scrap at backyard smelter sites. The limite lead smelting in Ebony Vale is probably due par direction near the established smelter and to dilu contamination by the more recent grading of l. community. In addition, cottage smelters were foun older, poorer Red Pond community.

The blood lead–soil lead relationship for child Pond differed from that expected from guidelines a in developed countries. A model derived from surve smelters in the United States predicts a geometric m 11 µg dL^{-1} among children less than six years old a level of 500 ppm (Schilling and Bain, 1988). In c univariate model of blood vs. soil lead in Red Po predicts a geometric mean PbB of 32 µg dL^{-1} amo under age six at a soil lead level of 500 ppm. In rev from published studies, Madhavan *et al.* (1989) pr 'worst case' relationship for the blood lead relationship an 8.6 µg dL^{-1} increase in PbB above b per 1,000 ppm of lead in soil. From the multivariat Red Pond children under age 6, the minimum predic in geometric mean blood lead above background is at a soil lead level of 1,000 ppm.

It is possible that children in Red Pond ingest more lead from soil than children in developed co temperate climates because of differences in outdoors, hygiene, and nutrition. Duggan and In

proposed such factors as explaining differences in the blood lead–soil lead relationship found in different settings in developed countries. One would expect even greater differences in these determinants of lead exposure and absorption in developing countries.

Differences in soil lead–blood lead relationships observed across studies may, of course, be due to other factors, such as differences in sampling methods, incomplete or inaccurate measurement of non-soil exposure sources, and differences in bioavailability of lead from different sources (Duggan and Inskip, 1985). Soil characteristics may also affect bioavailability; sandy soils with low organic content (as might be found in the tropics) would be expected to adsorb lead less well than clay soils rich in organic matter (Chancy *et al.*, 1988). Methodologic factors could also account for some of the discrepancy between the findings of this study and those reported near other smelters. For example, air lead levels could not be measured during smelter operation, and their impact on blood lead levels could not be assessed. In addition, because of small sample size and collinearity between many study variables, some variables may contribute to environmental or blood lead but not be statistically significant in multivariate models. Finally, some unavoidable measurement error in characterizing certain exposures, such as dust lead, may have diluted real associations.

Additional studies of lead-exposed children in developing countries are needed before firm conclusions can be drawn about the relative susceptibility of such children to lead poisoning. If such future studies are consistent with the blood lead–soil lead relationship we observed in Jamaican children, it would indicate that environmental health criteria for soil lead in developed countries may not be protective in developing countries.

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Estimating Childhood Multi-Media Lead Exposure: Expanded Exposure/Uptake/Biokinetic Model

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Abstract

Despite significant reductions over the past decade, lead exposure continues to be a problem for millions of children in the US. Minimizing further exposure to lead from its numerous and diverse sources is a priority of various regulatory components of the Environmental Protection Agency (EPA), as well as other Federal and State agencies. A critical step in assessing lead risks is the estimation of childhood lead exposure in the future under alternative regulatory scenarios. Using a wide variety of year- and age-specific data on lead concentrations in multiple media, exposure and activity patterns, absorption rates and biokinetics, an integrated uptake/biokinetic model was developed by EPA in its review of the lead National Ambient Air Quality Standard. The model can estimate blood lead distributions among childhood populations over time. It was validated using measured environmental and blood lead data around a primary lead smelter, and has been successfully applied to other point sources. An enhanced version of the model has been developed to deal with a wider variety of exposure situations, especially those at high levels. A personal computer (PC) compatible version is available for assessments of Superfund sites, paint lead abatement strategies, drinking water contamination and other problems.

Introduction

Major declines in lead exposure in the US continue to occur, due mainly to the gradual replacement of older lead-burning vehicles, the dramatic reduction of leaded gasoline's lead content and availability, the shift towards lead-free food cans, the ban of lead solder use in water supplies and increased corrosion control by public water suppliers. Because of its pervasiveness and persistence in the environment and its broad toxic properties, efforts by Federal, State and local governments will continue on further reducing lead exposures. These efforts will focus on drinking water, industrial facilities that process lead and its products, lead-painted housing and historically-contaminated soils.

Developing sound policy and strategies for such efforts requires evaluation of projected health impacts or benefits of alternative prevention and abatement measures. This paper describes the EPA's Integrated Exposure/Uptake/Biokinetic Model which is used to estimate risks among childhood populations exposed to different levels of lead from multiple sources and media.

Model Development

In 1986, EPA's Office of Research and Development published revised Air Quality Criteria for Lead (referred to as the "Criteria Document" or CD) which summarizes available information on lead exposure and health effects (US EPA, 1988). The original Cd was used in 1978 to set the National Ambient Air Quality Standards (NAAQS) for lead. The EPA's Office of Air Quality Planning and Standards (OAQPS), as part of its review of the lead NAAQS, developed three approaches for evaluating alternative standards (US EPA, 1989a):

(1) A 'disaggregate' model which combines separate empirical relationships, derived from epidemiological or clinical studies and multiple regressions model, between blood lead and lead intake from air, dust, soil, food and water.

(2) An 'aggregate' model which uses a directly applied mathematical relationship between air lead and blood lead, derived from community epidemiological studies, that includes contributions both from direct inhalation exposure and indirect exposures via deposition of lead particles and subsequent ingestion. Estimated contributions from non-air sources of lead exposures are derived for current and future years, based on nationwide data on gasoline usage, dietary lead concentrations and blood lead surveys.

(3) The uptake/biokinetic model which uses measured rates of absorption or 'uptake' of lead through different pathways (inhalation, ingestion) from experimental studies together with mathematical (biokinetic) modeling from lead balance studies to project either total body burden or the amount of lead in any of the physiological 'kinetic' compartments (*e.g.* blood, soft tissue, bone) at any time.

All of the methodologies account for the fact that air lead contributes both directly (via inhalation) and indirectly (via ingestion of deposited particles onto soils, dusts and crops) to total exposure, along with several other sources (*e.g.* solder in plumbing and food cans, historically-contaminated soils, lead-based paint). Adjustment is made for recent and continuing downward trends in gasoline, canned foods and drinking water. The disaggregate and aggregate models rely on relationships between blood lead and lead in different media derived from

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cross-sectional population studies. Further, these (A) approaches require an assumption that dust and soil concentrations are in equilibrium with air lead levels, and that the present air lead exposures reflect historic levels. The accuracy of these models thus depends on the study populations and site-specific environmental conditions that existed. Most of the studies were conducted in the 1970s and early 1980s when environmental lead loadings were much higher. Thus, the aggregate and disaggregate modeling approaches present 'snapshot' estimates which are less likely to provide accurate predictions given the significant trends in environmental lead levels, especially for children, whose exposure patterns, metabolism and physiology change rapidly.

The uptake/biokinetic model incorporates age-specific differences in exposure and biokinetics, and can be used to model cohorts of children from birth. The model allows explicit projections of future lead concentrations in various media, and in turn can be used to estimate impacts of these different changes on different age-groups of children. The flexibility of the uptake/biokinetic model in reflecting non-equilibrium lead exposures in children allows better estimation of changes in blood lead levels (or other tissue lead levels) over time in response to changes in environmental lead in rapidly developing young children compared to other models. For this reason, it was the focus of validation exercises described in the OAQPS staff report (US EPA, 1989a) and of case-study analyses of alternative lead which NAAQS described in the OAQPS staff paper (US EPA, 1989b). (Results of validation studies of the model using real world data collected near various lead point sources will also be presented in a subsequent paper.) EPA's Clean Air Science Advisory Committee reviewed the different exposure methodologies and supported these conclusions (Larson, 1989).

The model developed by OAQPS has since been extended using additional data on bone and blood-cell biokinetics, gut absorption and transfer of lead from mother to newborn. The model is currently programmed in a convenient DOS executable format for a wide variety of applications on the PC.

Model Description

The uptake/biokinetic modeling approach attempts to account for the following: (a) the amount of lead in the body at any one time is the product of dynamic interactions of partially offsetting processes of absorption, distribution, storage, mobilization and excretion; (b) these processes vary with the route and rate of exposure, a person's age, nutritional and health status and baseline exposure; (c) uptake from all sources by all absorption routes can be separately modeled, thus providing an estimate of the relative importance of atmospheric lead exposure, either directly or indirectly, to the total lead body burden; and (d) past and future trends in environmental lead levels due to different control efforts and regulations are important determinants of projected exposures.

A discussion of lead's absorption, excretion, retention and distribution within the body under different exposure and physiological conditions is necessary background to the uptake/biokinetic model, and is provided in Chapter 10 of the CD (US EPA, 1988).

The model contains three separate components: (1) the exposure model uses estimates of lead concentrations in air, outdoor soil, indoor dust, water and food to estimate lead intake or consumption (inhalation, ingestion) from various sources; (2) the uptake model uses estimates of the rate of lead into the body from different sources and media; and (3) the biokinetic model uses the lead uptakes to estimate concentrations of lead in blood, bone and soft tissues.

Estimates of Lead Intake and Uptake

Lead intake is defined as the amount of lead brought into the body (*i.e.* consumed) by inhalation or ingestion. For each exposure source, lead intake is calculated as:

Intake = Consumption × Lead concentration

Depending on what exposure scenario is being evaluated, lead concentrations in different sources may be actual measurements or estimates based on past or projected trends.

Lead uptake is the amount of lead absorbed into the blood-plasma system for distribution into various body compartments or for excretion, and is calculated as:

Uptake = Intake × Absorption factor

Uptake estimates from air, soil, dust, food and water are calculated and used as input to the biokinetic model.

A description of the relevant data and assumptions used in estimating the different exposure parameters and their default values and absorption rates is given in the OAQPS staff report (US EPA, 1989a). The extensive literature review necessary in documenting these parameter estimates is presented in that report. 'Default' values used in the current version of the model are presented below for illustrative purposes. Some parameters in the model are assigned lower and upper bound values defined by the range of available data and judgments of reliability and relevance. Midpoint estimates of the various parameters are considered best estimates and are generally incorporated into the exposure analyses used by the model. As with any of the parameters, sensitivity analyses of user-specified parameter values are convenient. Users should be an integral part of the model's application. Some parameters, such as soil ingestion rates, soil absorption factors and house-dust concentrations are highly influential in predicting childhood blood lead levels. Where possible, users should attempt to collect site-specific data on environmental lead concentrations in various media, including soil, dust, air and drinking water. EPA is developing additional guidance on use of the model which will explain how to collect and use environmental lead data from specific sites.

Air lead intake

Air lead intake is calculated in several steps:

(1) Outdoor and indoor lead concentrations are estimated. Indoor air lead can be estimated by multiplying ambient air concentrations by 0.3–0.8 if modeling a typical urban area dominated by relatively fine lead particles (US EPA, 1986, Table 7–6). If a lead smelter or other point source is present, a factor of 0.3 is derived from the literature (Cohen, 1980).

(2) Time-weighted average concentrations of lead in air are calculated using indoor/outdoor activity patterns. Time spent outdoors varies among young children depending on season, geographical location and family behavior patterns. Consistent estimates appear in the literature (Pope, 1989) and were confirmed by informal surveying of parents.

Table 1 *Age-specific exposure parameter values for lead uptake model.*

Parameter	Age group (years) <1	1–2	2–3	3–4	4–5	5–6	6–7
Hours spent outdoors	1–2	1–3	2–4	2–5	2–5	2–5	2–5
Ventilation rate (m^3 day^{-1})	2–3	3–5	4–5	4–5	5–7	5–7	6–8
Dietary lead intake (μg day^{-1})	7.5	8.9	10.4	10.7	10.8	11.3	11.9
GI absorpuon rate (%)	42–53	42–53	30–40	30–40	30–40	30–40	18–24
Dirt ingestion (mg day^{-1})	0–85	80–135	80–135	80–135	70–100	60–90	55–85

1989a), and are summarized in Table 1.

(3) Air lead intake is estimated by multiplying time-weighted air lead concentrations by the volume of air respired. Average ventilation rates were constructed from measurements reported in the literature and scaling factors based on body size and lung capacity (Altman and Dittmer, 1971, 1972; Nutrition Foundation, 1982, 1985; Phalen *et al.*, 1985; see Table 1).

Air lead uptake

Only a portion of inhaled lead is deposited in the lungs and subsequently absorbed into the bloodstream. The deposition efficiency of lead particles depends primarily on their size, and on physiology and rate of breathing of the individual. Some particles not deposited will move up the airways and be swallowed. Available data on lead particle size distributions, particle deposition patterns in the lung and respiratory absorption of lead particles were used to estimate deposition efficiencies of airborne lead particles in young children (Cohen, 1987). A respiratory deposition/absorption rate of 25–45% is calculated for young children living in non-point source areas, while a rate of 42% is calculated for those living near point sources of lead.

Total lead uptake from the air is the product of total intake and the lung deposition/absorption factor.

Dietary lead intake

The Multiple Source Food Model was developed in the 1986 CD and extended in the OAQPS exposure report (US EPA, 1989a) using the most recent data on lead in different foods from solder, air lead deposition on crops and soils and eventual uptake, trends in canned food manufacturing, gasoline lead emissions and lead in drinking water, and age-specific dietary patterns. Age-specific dietary lead intakes estimated for US children for 1990–1996 are given in Table 1.

Given the wide spatial and temporal distribution of food in the US, it was assumed that most people receive roughly the same levels of lead in their diet. However, there can be considerable variability due to such things as local contamination of garden vegetables or frequent use of imported canned foods that may be sealed with lead solder. Perhaps of even greater significance is the considerable variability in exposures to lead in drinking water which can vary from city to city or house to house depending on source water characteristics and the age and type of materials in the distribution system and household plumbing. Some drinking water coolers in schools may also be of concern because of lead-soldered parts or lead-lined tanks. The model allows alternate factors and values for food and drinking water to be included according to user specifications. Allowance is made for differences in garden crops, meat (hunted game), imported canned food use, lead levels in tap water that is either first-draw or flushed and in water fountains.

Dietary lead uptake

Only a portion of ingested lead is absorbed into the bloodstream from the gastrointestinal tract (GI) or gut. This is dependent upon the composition of the diet and physiological and nutritional status of the individual. Based on balance studies on infants and adults of lead in diet and excreta, gut absorpuon rates were estimated for intermediate ages of children (see Table 1).

These rates do not reflect the wide degree of inter-subject variability observed in the literature nor other factors that influence absorption in children (fasting conditions, deficiencies in calcium, iron, protein, *etc.*). As for other sources of variability, this is accounted for in calculating populauon distributions of blood lead levels around estimated average blood lead levels. The model will allow alternate gut absorpuon rates for lead in diet or lead in soils or paint (see below) to be specified.

Total dietary lead uptake is calculated as the product of dietary intake by the gut absorpuon rates.

Dust and soil lead intake

Concentrations of lead in soil and dust. Ingestion of lead in street and household dusts and in outdoor surface soil (*e.g.* the top 2 cm) during normal hand–mouth activity is a major source of uptake in young children (and worse in children with pica). Perhaps more than any other exposure source, it is desirable to input measured concentrations of lead in these media into the model for reliable blood lead estimates.

Since future scenarios under alternative lead NAAQS were being assessed, the OAQPS exposure report (US EPA, 1989a) estimated soil and dust lead levels that would be associated with different air lead concentrations. Many complex variables influence soil and dust lead levels, such as deposition rates, chemical and physical characteristics of the lead particles and soils, topographic and meteorological conditions, frequency

of street washings and precipitation runoff, background dust concentrations and transport of dusts and soils into homes and buildings. Given the available data, changes in soil and dust lead were directly modelled using regression analyses from studies in which lead in air (PbA), soil (PbS) and/or dust (PbD) was measured at over 40 sites near and in broad spectrum of homes and neighborhoods, given the nature of the analysis, emphasis was on data collected near operating primary and secondary lead smelters, battery plants and other non-ferrous smelters (zinc, copper).

The derived linear relationships, given below and discussed in detail in Appendix B of EPA, 1989, are for predicted geometric means depending on the level of available information.

Predicting PbS (ppm) when PbA (mg m^{-3}) is available:

Geometric mean PbS = 53 ppm + 510 (PbA)

Predicting PbD (ppm) when only PbA is available:

Geometric mean PbD (ppm) = 60 ppm + (PbA)

Predicting PbD when both PbA and PbS are available:

Geometric mean PbD = 31 ppm + 638 (PbA) + 0.364 (PbS)

These relationships reflect baseline, historical accumulations of gasoline and point source emissions and paint lead. Account was made for the fact that indoor dust lead is related not only to paint lead but also to lead tracked in from outdoors. Data on time scales for soil and dust lead changes are incomplete. The monitoring data sets used to derive the coefficients for these equations are assumed to be in dynamic equilibrium at the time of sampling. In using these equations, the inherent uncertainties in making this assumption should be recognized. Lead in undisturbed soil matrix persists for an extremely long time, but soil lead concentrations in disturbed (especially urban) environments appear likely to change, on average, over periods of a few years to reflect changes in surface deposition. Interior dust lead concentrations will likely change over similar time periods in response to air lead changes, depending on interior–exterior access and interior recirculation or removal of dust.

Concentrations of lead in dust and soil due to flaking, peeling or 'powdering' of lead in paint used in the model should be based on measurements for accurate modelling. There are inadequate data to make default estimates of lead inputs from paint, given the considerable variability depending on housing age, extent of deterioration, layers of paint, family behaviors and climate. The model allows separate estimates of paint lead contributions to indoor dust and soil as well as direct inputs into children via ingestion of paint chips.

Time-weighted concentration of lead in dust and soil. The time-weighted concentration of lead in dust and soil (dirt) that a child is exposed to is computed using indoor/outdoor activity estimates given in Table 1 by:

$$\frac{(\text{PbS} \times \text{time spent outdoors}) + (\text{PbD} \times \text{time spent indoors})}{12 \text{ (average hours child is awake)}}$$

Amount of dirt ingested by children. The amount of dirt that children typically ingest was estimated in the OAQPS exposure report (US EPA, 1989a) from available mass-balance studies on children in which relatively non-absorbed elements in soil (aluminum, silicon, titanium) were used as tracers (Binder *et al.*, 1986; Clausing *et al.*, 1987; see Table 1). More recent studies that included specific examination of tracer-element metabolism and dietary intake of these elements support for the earlier ingestion estimates (Calabrese 1989; Davis *et al.*, 1990). Adjustments can be exp analyses continue on these newer studies.

The ranges represent average exposure estimates not reflect children with pica. Children with pica with r hand–mouth activity or who deliberately ingest paint paper, dirt and other non-food items will be exp considerably amounts of lead compared to children w inadvertently ingest foreign substances. It is estima between 6 and 12% of young children have pica, althou studies report prevalence rates as high as 35–50 among olds (US EPA, 1989a). Complete direct data on ingestion among pica children are not available, alt worse case estimate of 1 g day^{-1} has been suggested (1989a).

Lead intake from dust and soil is computed by mu the time-weighted average concentrations by the estim ingestion rates.

Uptake of lead in soil and dust

Based on experiments on rats and *in vitro* simulatio solubilization of soil and paint lead particles in the stor 1986 CD estimates that 30% of lead ingested in dust a absorbed in a child. There is some evidence that lead a through the gut may follow a non-linear process, e evident at high doses (US EPA, 1988). In fact, improv the uptake/biokinetic model estimates to measured b levels in children living near a lead smelter resulted absorption rate of 0.3 was assumed for children livin a one-mile radius from the smelter, and a rate of assumed for children living within one mile. A clos resulted when a rate of 0.25 was used for the entire p Whether the non-linearity in absorption rates is exp intake levels, soil lead speciation or some phys phenomenon requires additional research.

Recent data collected in Cincinnati and Colorad that the bioavailability of various chemical and physi of lead in the environment can significantly affect b predictions (Bornschein *et al.*, 1989). An accompany in this volume discusses the geochemical factors that lead bioavailability (Hemphill *et al.*, 1990 uptake/biokinetic model will be modified to be lin chemical speciation/GI absorption model so that different soil matrices, particle sizes and chemical forn analyzed. Also, research is underway to develop rela between soil lead bioavailability and soil lead particle and speciation. Until that time, the default GI absor for soil/dust lead near a lead point source is set at 0.2 of 0.3 is suggested for lower-level exposure situatio from a point source.

Total lead uptake from dust and soil is ob multiplying lead intake by the GI absorption rates.

Lead Biokinetic Model

The biokinetic section of the uptake/biokinetic model lead uptakes totaled from air, food, water, soil a calculate the amount of lead excreted and stored i body compartments on a monthly basis. The basic a to consider lead in dynamic equilibrium in

compartments. Equations are formulated in terms of transition times between compartments that represent well-mixed kinetically homogeneous physiological pools, organs or tissues grouped together and that share lead distribution and transfer (*i.e.* biokineuc) properties. The body compartments in the biokinetic section of the uptake/biokineuc model include a blood pool, skeletal bone, the kidneys, the liver and an 'other' soft tissue pool.

The basic assumption of the biokinetic models is that the mass of lead in each of the compartments changed according to a system of coupled first-order, linear differential equations with age-dependent fractional transfer rates. Such models predict that when the lead intake changes from one constant level to another, there is a directly proportional change in the mass of lead in each compartment and the attainment of a new equilibrium. The rates and magnitudes of these changes are dependent upon the rates of lead flux in the tissues, and can theoretically be calculated from a compartmental model of the appropriate parameters. Support for a first-order kinetic model for lead metabolism is demonstrated by calculations using first-order models of soft tissue and bone concentrations of lead and other elements (calcium, stronuum, radium) that fit human measurements, as well as by using more complex models (Harley and Kneip, 1985).

The biokinetics of lead in adults have been determined from long-term balance clinical studies and lead isotope tracer experiments (US EPA, 1988). The basic biokinetic model used here for children was developed at New York University (NYU) from data obtained in controlled single dose and chronic lead exposures of infant and juvenile baboons (Mallon, 1983; Kneip *et al.*, 1983). Dynamic blood measurements and steady-state blood and organ lead measurements were closely fitted to predicted concentration of lead in blood, liver, kidney and bone (the four compartments in which 95% of total body lead is contained). Baseline information on human metabolism and organ size and growth patterns were applied in computer simulation that was successfully validated using human autopsy data.

The model parameters were revised using measured metabolic data for each organ (*e.g.* bone turnover rates) for children, and were used to simulate organ lead burdens and concentrations in children with constant lead exposure from birth (Harley and Kneip, 1985). Although complete model validation is not possible, the revised model is consistent with experimental data on blood lead accumulation following dietary lead uptake among infants, and skeletal accumulation in adults following controlled exposures (US EPA, 1989a).

Adjustments to the model were made to include the propogation of maternal lead during pregnancy that persists throughout childhood (US EPA, 1989a). This adjustment was done using another kinetic model fit to blood-lead data collected longitudinally in young children from birth to 27 months (Succop *et al.*, 1987).

Since completion of the OAQPS exposure report, the NYU model has been extended in several directions based on recent data. These changes are summarized below:

(1) *Additional compartmentalization of the blood pool/kinetic non-linearity in uptake of lead by red blood cells at high concentrations.* The plasma and extra-cellular fluid are the central distribution pool for lead in the body. Earlier analyses regarded whole blood as the central pool, but recent studies have shown that the red blood cells, which hold most of the lead in the blood, have limited capacity for lead and should be regarded as a saturable peripheral pool (Marcus, 1985; O'Flaherty *et al.*, 1989). In some individuals, lead exposure may induce the formation of lead-binding erythrocyte proteins (reducing the toxicologically significant plasma-lead concentration) (US EPA, 1988). Blood lead is likely to follow a non-linear kinetic process (Marcus, 1985; Marcus and Schwartz, 1987), although these non-linearities are not likely to be important at whole-blood lead concentrations less than 25 $\mu g\ dL^{-1}$ in adults and 20 $\mu g\ dL^{-1}$ in children. To allow greater resolution of lead transfer among tissues and flexibility to deal with high-level 'non-linear' uptake rates, the 'blood' pool was divided into plasma, extra-cellular fluid and red blood cells, based on available *in vitro* and experimental data on lead distribution. Non-linear equations for lead uptake by red blood cells at high concentrations were developed from these data.

(2) *Additional compartmentalization of the bone pools.* The 'bone' pool was divided into two compartments, the cortical or compact bones *versus* the trabecular or cancellous bones. In adults, cortical bone is about 80% of the bone material and retains lead for many years. In young children, however, the trabecular bone material develops very rapidly and constitutes a relatively large reservoir of lead that turns over relatively rapidly (1–2 years) compared to the compact cortical bone material. The relatively large bioavailability of lead in young children suggests the need to regard the bone as a 'slower' pool for endogenous lead recycling, but not as an inert 'sink'. Available weight and growth data of skeletal components were used in adjusting the model for cortical and trabecular bone.

(3) *Kinetic non-linearity in gut absorption of ingested lead at high levels.* As noted earlier, there is some evidence that gut absorption may be kinetically non-linear (Aungst and Fung, 1981). The gut lead concentrations at which active transport mechanisms are 50% saturated appear high relative to typical human intake (US EPA, 1988). However, recent analyses of the relationship between blood lead and water lead in young children indicate curvilinearity at fairly low water lead concentrations (Marcus, 1989; Maes *et al.*, 1990). Equations for partially saturable lead absorption will be included in the model, along with equations that will allow modification of lead uptake for nutritional factors (*e.g.* calcium deficiency), soil lead particle size and speciation and soil matrix.

As discussed earlier, further refinement of the model continues to be explored to account for differential bioavailability of various physical and chemical forms of environmental lead.

(4) *Fetal lead exposure through the mother.* The transfer of lead during pregnancy across the placental membrane not only poses risks to the fetus but becomes part of the developing child's body burden. Prenatal lead burdens stored in fetal tissues are eliminated over time: 1–2 months for soft tissues (Ryu *et al.*, 1983), and possibly years for prenatal skeletal lead burdens (Succop *et al.*, 1987). Prenatal lead exposure has been associated with persistent postnatal psychomotor and neurobehavioral deficits (US EPA, 1988). As noted above, the current version of the Exposure/Uptake/Biokinetic Model does account for the propagation of prenatal lead burden through infancy. Maternal blood lead can be entered as an independent variable.

We are developing refinements to the modeling of

maternal/child lead transfer which will include time-dependent changes during pregnancy. This option will use regression models for adult populations derived from community studies in the literature. The same air and water lead exposures will be applied that are used for the infant, along with options for maternal occupational or other lead exposures. Maternal blood lead will increase with age, reflecting increased resorption of lead from the skeleton. Maternal blood lead will decrease during most of the nine months of pregnancy due to the growth in maternal plasma volume.

Fetal blood lead will be assumed to be proportional to maternal blood lead. A ratio derived from over 30 different studies consistently indicate a ratio of 0.8 to 0.9 between umbilical cord blood lead and maternal blood lead levels (US EPA, 1989a). It will be assumed that tissue lead concentrations in the newborn are proportional to the cord blood level. Ratios of average tissue lead concentrations to blood lead concentrations derived from autopsy data on deceased infants (Barry, 1981) will be used to set initial conditions for the newborn.

Future developments may include a detailed biokinetic model for maternal blood lead that is comparable to the childhood model. Since the mother is the only portal of entry for the fetus, a descriptive model for maternal blood lead is likely to be adequately predictive of prenatal exposure.

Calculating Blood Lead Distributions

Because most of the data input to the uptake/biokinetic model (as well as the aggregate and disaggregate models discussed earlier) are generally average estimates, blood lead estimates are considered to represent population averages. The distribution of blood lead levels among children is broad because there is a distribution of environmental lead concentrations, a distribution of behavior patterns that affect lead intake and a distribution of biological absorption and excretion rates. In assessing protectiveness of alternative regulations or abatement strategies, it is necessary to determine the blood lead distribution across defined population groups so that children with the greatest potential for adverse response to a given lead exposure can be considered.

Consistent with measurements of other materials in tissues of human populations, blood lead levels for any relatively homogeneous population closely follow a lognormal distribution (US EPA, 1988). A lognormal distribution is completely specified by its geometric mean (GM) and geometric standard deviation (GSD). As EPA did in setting the lead NAAQS in 1978, the uptake/biokinetic model program calculates percentiles of a blood lead distribution (*e.g.* median, 99th percentile) around the estimated mean blood lead level by using the following equation:

$$PbB = GM\,(GSD)^{z}$$

where GM = geometric mean blood lead (estimated directly from the uptake/biokinetic model)

z = the number of standard deviations

PbB = value of blood lead at z standard deviations

In terms of quality control and sample size, the NHANES II study of 1976–1980 provides the best available data on nationwide blood lead levels (US EPA, 1988). Estimates of GSDs for various subgroups of young children from NHANES II range between 1.3 and 1.4. A GSD for young children was estimated at 1.42 after removing the variance levels attributable to air lead exposure. While variations in background non-air lead exposure 1988). Assessment of studies conducted aroun primary or secondary lead smelters coincidentall identical average GSD value (US EPA, 1989a).

Selection of a GSD value to model popula future lead exposure scenarios depends on a regarding future variance. Total lead exposure can to continue to decline for most people due to downward trends in canned foods, the nationwide solder in plumbing, new EPA drinking-water limits continued decline of lead in air and perhaps incre awareness regarding lead exposure hazards an avoidance measures. All of these measures shoul only in lower mean baseline lead exposures, but p importantly, in fewer high-level exposure situatio variance in blood lead levels. Quantifying such estimating a future GSD is difficult. Important infor be derived from NHANES III which will be compl Until then, it is suggested that a range of GSI modeled (approximately 1.3 to 1.4) with use conservative 'best' estimate.

The PC software application of the uptak model graphs probabilities of different blood l trations *versus* probability so that the percentage above different target blood lead levels of concern 25 μg dL^{-1}) can be easily estimated.

Discussion

Ongoing regulatory efforts by different components control concentrations of lead in air, water and soil a need to model blood lead concentrations among populations that delineate specific routes of n exposure. Results of validation exercises indica uptake/biokinetic model performs well in predicting levels in children living near lead point sources wit moderate environmental lead loadings. There is c interest in using the model to estimate blood lea children exposed to high-intensity lead hazards deteriorating lead paint or heavily contaminated historical deposition near major urban roadways smelters or mines. Additional refinements to t particularly the incorporation of non-linearit relationship between lead exposure and blood lead, made and are continuing to allow application to extr exposure scenarios (*e.g.* >4,000 ppm). Validation using data collected around lead mines are underway provide useful information in further refining the m

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PITCON '92

9–13 March 1992. 43rd Pittsburgh Conference and Exposition on Analytical Chemistry and Applied Spectroscopy. New Orleans, LSA.
Contact: Pittsburgh Conference, 300 Penn Center Blvd., Suite 332, Pittsburgh, PA 15235-5503, USA.

Redox Transformations

5-10 April 1992. Redox Transformations of Inorganic and Organic Species in the Environment. ACS National Meeting, Division of Environmental Chemistry Symposium. San Francisco, CA, USA.
Contact: J. Westall, Department of Chemistry, Oregon State University, Corvallis, OR 97331-4003, USA.
Phone: 503 737 2591.

Biogeochemistry

5-10 April 1992. Biogeochemistry of Terrestrial Systems. ACS National Meeting, Geochemistry Division Symposium. San Francisco, CA, USA.
Contact: W.H. Orem, USGS, 923, National Center, Reston, VA 22092, USA. Phone: 703 648 6273.

Aquatic Chemistry

5-10 April 1992. Aquatic Chemistry. ACS National Meeting, Division of Environmental Chemistry Symposium. San Francisco, CA, USA.
Contact: C.R. O'Melia, Department of Geography and Environmental Engineering, John Hopkins University, Baltimore, MD 21218, USA. Phone: 301 338 7102.

Isotopes

12-15 April 1992. Isotopes in Environmental Geochemistry and Health. 10th European Meeting of the Society for Environmental Geochemistry and Health. University of Edinburgh, UK.
Contact: Dr J.G. Farmer, Department of Chemistry, University of Edinburgh, King's Buildings, West Mains Road, Edinburgh EH9 3JJ, UK. Phone: 031 650 1000. Fax: 031 650 4743. Telex: 727442 (UNIVED G).

Reproductive Toxicology

28 April 1992. Reproductive Toxicology. RSC Toxicology Group together with Health, Safety and Environment and Women Chemists Committees. London, UK.
Contact: P A Sim, Gascoinge Secretarial Services, 25 Southfield Drive, Huxlemere, High Wycombe, Bucks HP15 7HB, UK.
Phone 0494 713664. Fax: 0494 714516.

Reference Materials

11-14 May 1992. 5th International Conference on Biological and Environmental Reference Materials (BERM-5). Aachen, Germany.
Contact: Dr W.R. Wolf, Nutrient Composition Laboratory, US Department of Agriculture, Beltsville, MD 20705, USA.

Water Quality

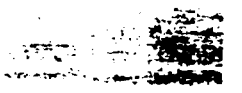
24–30 May 1992. Water Quality International '92, 16th Biennial Conference and Exhibition of the International Association on Water Pollution Research and Control (IAWPRC). Washington, DC, USA.
Contact: J.W. Patterson, c/o CAPS Ltd, 50 green Bay Road, Box 406, Lake Bluff, IL60044, USA.
Phone: 708 234 2353. Fax: 708 234 2844.
OR: Anthony Milburn, IAWPRC, 1 Queen Anne's Gate, London SW1 9BT, UK. Phone: 071 222 3848. Fax: 071 222 1197.

Trace Elements

25-29 May 1992. International Conference on Trace Elements in Health and Disease. 3rd Conference of International Society for Trace Elements Research in Humans (ISTERH) and 4th Nordic Trace Elements (NTES) Conference. Stockholm, Sweden.
Contact: ISTERH/NTES 1992, Dr L-O Plantin, Clinical Research Centre, Huddinge Hospital, S 141 86 Huddinge, Sweden.
Phone: 468 746 5568. Fax: 468 746 7483.

Environmental Sensing

22-26 June 1992. International Conference on Environmental Sensing- Monitoring Toxic Chemicals and Biomarkers. Berlin, Germany.
Contact: EUROPTO, c/o Direct Communications, Xantener Strasse 22, D-1000 Berlin, 15, Germany.
Phone: 49 30 883 9507. Fax: 49 30 882 2028.



Metal Ions in Biological Systems

8-12 July 1992. EUROBIC 1. Metal Ions in Biological Systems. Incorporating SAMBAS IV and SIMBIC VI. Royal Chemistry, Dalton Division and Inorganic Biochemistry Discussion Group. University of Newcastle Upon Tyne, UK.
Contact: Dr J F Gibson, The Royal Society of Chemistry, Burlington House, Piccadilly, London W1V 0BN, UK.
Phone: 071 437 8656. Fax: 071 437 8883. Telex 268001.

Copper and Zinc Triads

13-16 July 1992. 1st International Conference on Copper and Zinc Triads. Includes biological and environmental Edinburgh, UK.
Contact: Dr J F Gibson, The Royal Society of Chemistry, Burlington House, Piccadilly, London W1V 0BN, UK.
Phone: 071 437 8656. Fax: 071 437 8883. Telex 268001.

Aquatic Plant Control

12–17 July 1992. International Symposium on the Biology and Control of Aquatic Plants. Daytona Beach, Florida, US.
Contact: Dr George Bowes, Botany Department, University of Florida, Gainesville, FL 32611, USA.

Agriculture and the Environment

16–18 July 1992. Chemistry, Agriculture and the Environment. Surrey, UK.
Contact: Dr D. Stevenson, The Robens Institute of Health and Safety, The University of Surrey, Guildford, Surrey GU2
Phone: 0483 509220. Fax: 0483 503517.

Coordination Chemistry

19–24 July 1992. 29th International Conference on Coordination Chemistry. Lausanne, Switzerland.
Contact: 29th ICCC Secretariat, AKM Congress Service, Clarastrasse 57, PO Box, CH–4005, Basel, Switzerland.

Analytical Chemistry and Mining

2–7 August 1992. 3rd International Symposium on Analytical Chemistry in the Exploration, Mining and Processing of
Sandton, South Africa.
Contact: Symposium Secretary, Mintek, Private Bag X3015, Randburg 2125, South Africa.

Lead and Children

23-28 August 1992. Lead poisoning in Children: Exposure Abatement and Programme Issues. ACS National Meeting, D
Environmental Chemistry Symposium. Washington, DC USA.
Contact: J J Breen, Field Studies Branch, USEPA, Office of Toxic Substances, (TS-798), 401 M St. SW, Washington D
USA. Phone: 202 382 3569.

Analytical Chemistry

20–26 September 1992. International Conference on Analytical Chemistry. University of Reading UK.
Contact: Secretary Analytical Division, The Royal Society of Chemistry, Burlington House, London W1V 0BN, UK.
Phone: 071 437 8656. Fax: 071 437 8883. Telex: 268001.

Analytical Chemistry

5-11 September 1993. Euroanalysis VII, European Conference on Analytical Chemistry. Includes environmental analysis. U
of Edinburgh, UK.
Contact: Miss P E Hutchinson, Analytical Division, The Royal Society of Chemistry, Burlington House, Piccadilly,
W1V 0BN, UK. Phone: 071 437 8656. Fax: 071 743 1227. Telex 268001.

Analytical Environmental Chemistry

26 September–1 October 1993. 12th Australian Symposium on Analytical Chemistry incorporating the 3rd Environmental C
Conference. Perth, Western Australia.
Contact: 12 AC, The Conference Office, University of Western Australia, Nedlands, WA, Australia 6009.

Nutrition

26 September–1 October 1993. XV International Congress of Nutrition – Nutrition in a Sustainable Environment. Adelaid
Australia.
Contact: The Secretariat, XV International Congress of Nutrition, CSIRO Division of Human Nutrition, PO Box 10041
Street, Adelaide, SA, Australia 5000. Phone: 61 8 224 1800. Fax: 61 8 224 1841.

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Journal: Guy, R.D. and Chakrabarti, C.L. 1976. Studies of metal-organic interactions in model systems pertaining to natural waters. *Can. J. Chem.*, 54, 2600-2611.

Book: Kabata-Pendias, A. and Pendias, H. 1984. *Trace Elements in Soils and Plants*. CRC Press, Florida.

Yamagata, N. 1975. Cadmium in the environment and in humans. In: Tsuchiya, K. (ed.), *Cadmium Studies in Japan*, pp.19-43 Elsevier, Amsterdam.

Report: Royal Commission on Environmental Pollution. 1983. *Lead in the Environment*. Ninth Report. HMSO, London.

Published conference: Balasooriya, I., Pauliraj, P.J., Abeygunawardena, S.I. and Nanayakkara, C. 1984. The Biology of the water Hyacinth: Physico chemical properties of the water supporting, *Eichhornia crassipes* (MART.) Solms. In: Thyagarajan, G. (ed.), *Proceedings of the International Conference on the Water Hyacinth*, 7-11 February 1981, pp.318-333. UNEP, Nairobi.

Thesis, unpublished report or conference: Giles, S. 1976. How fertiliser works. PhD thesis, University of London.

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